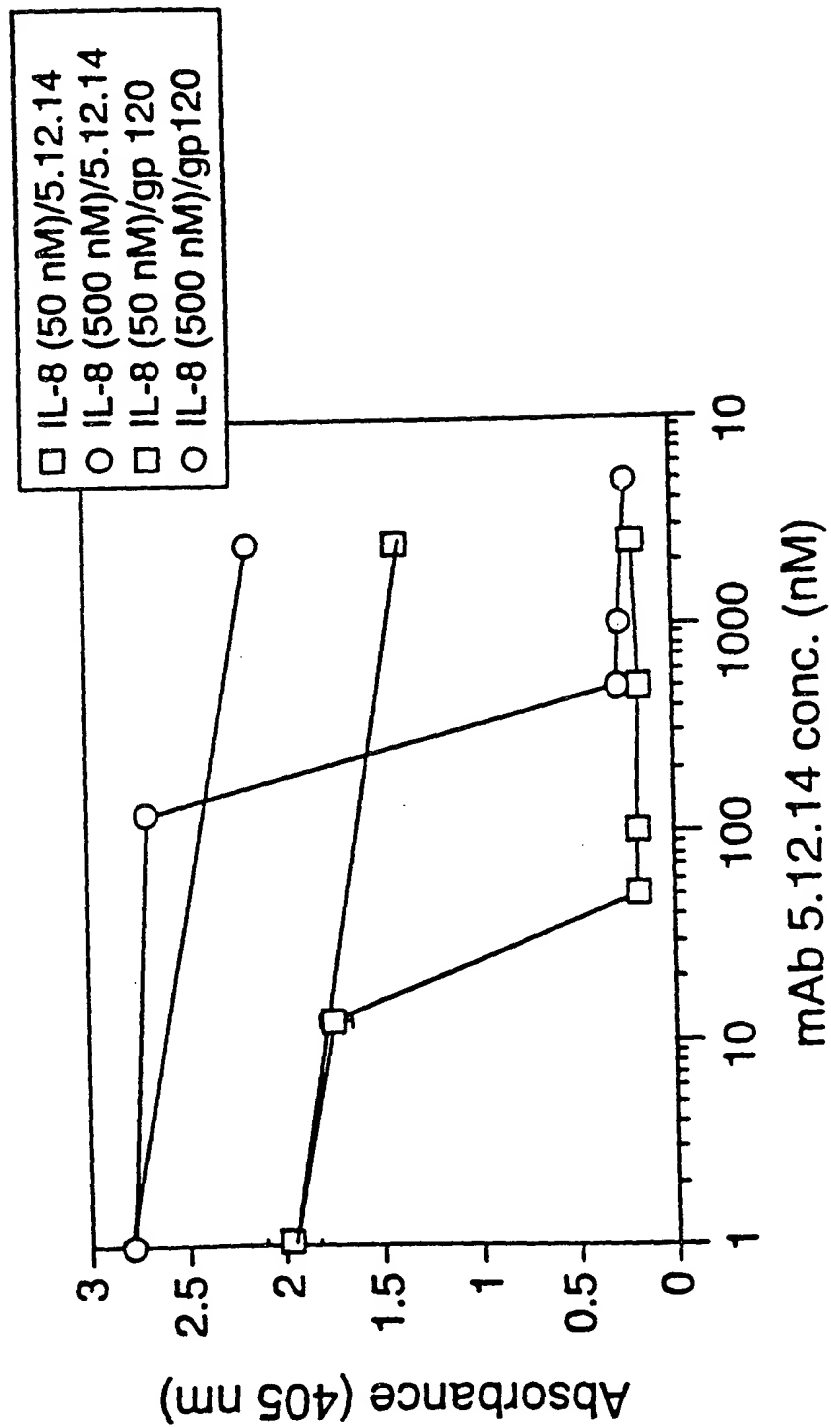
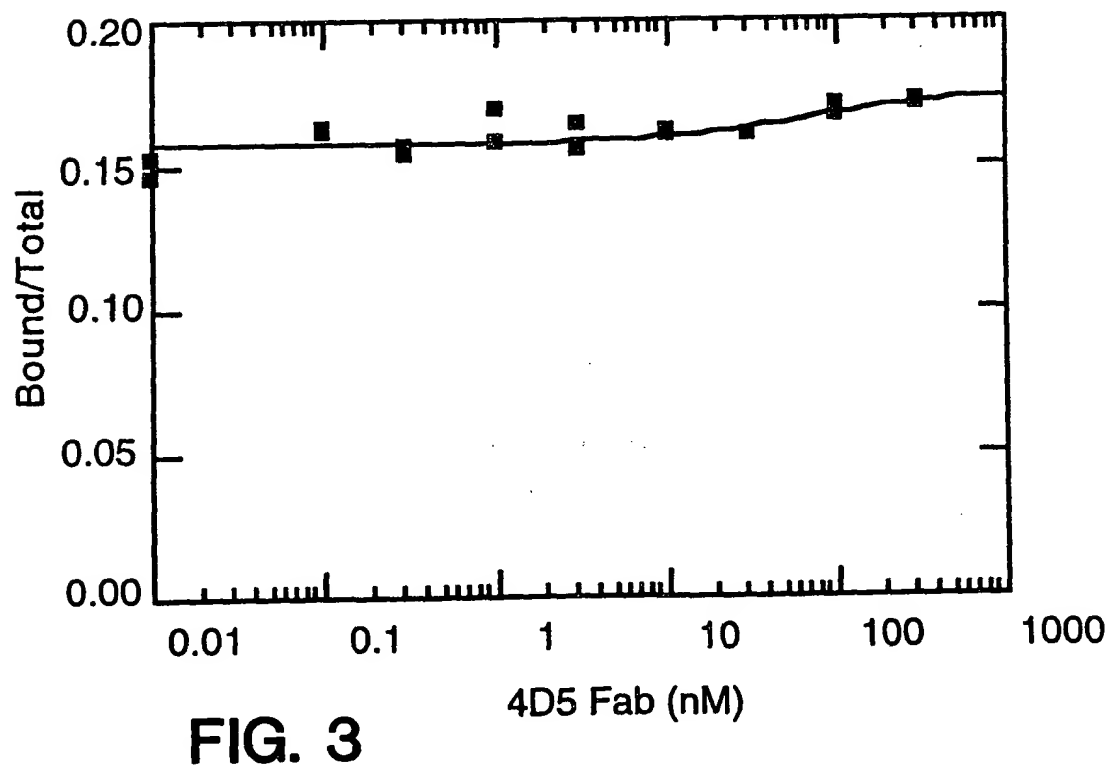
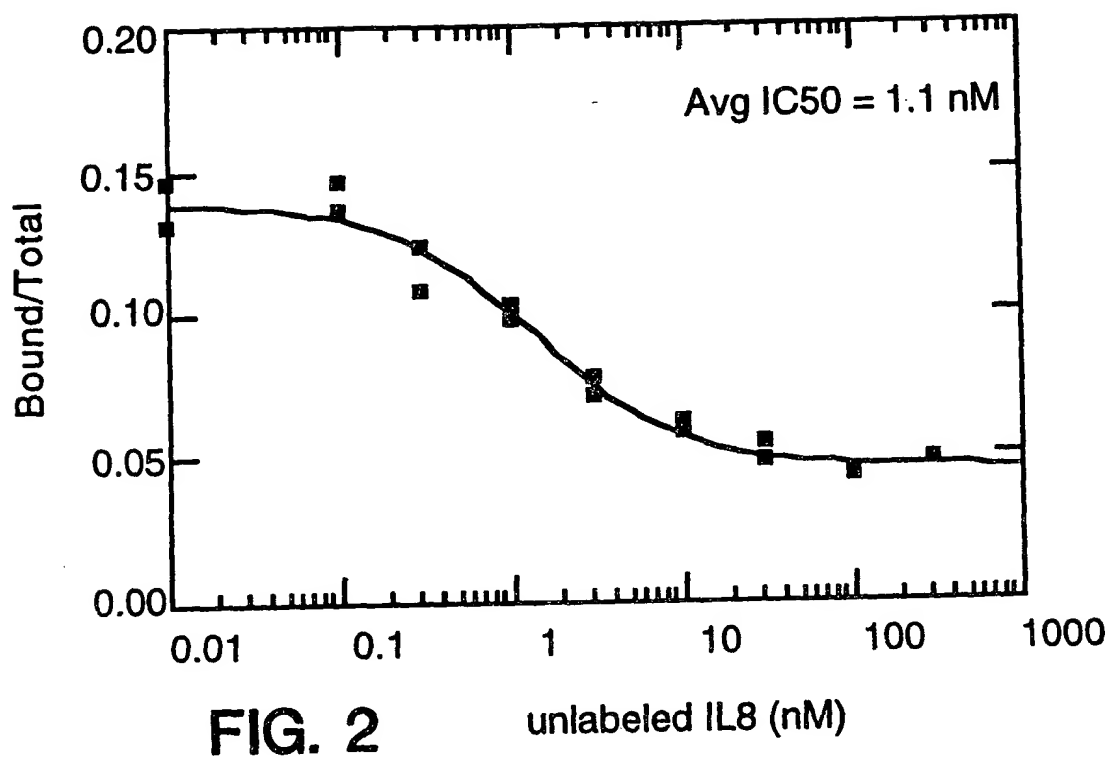
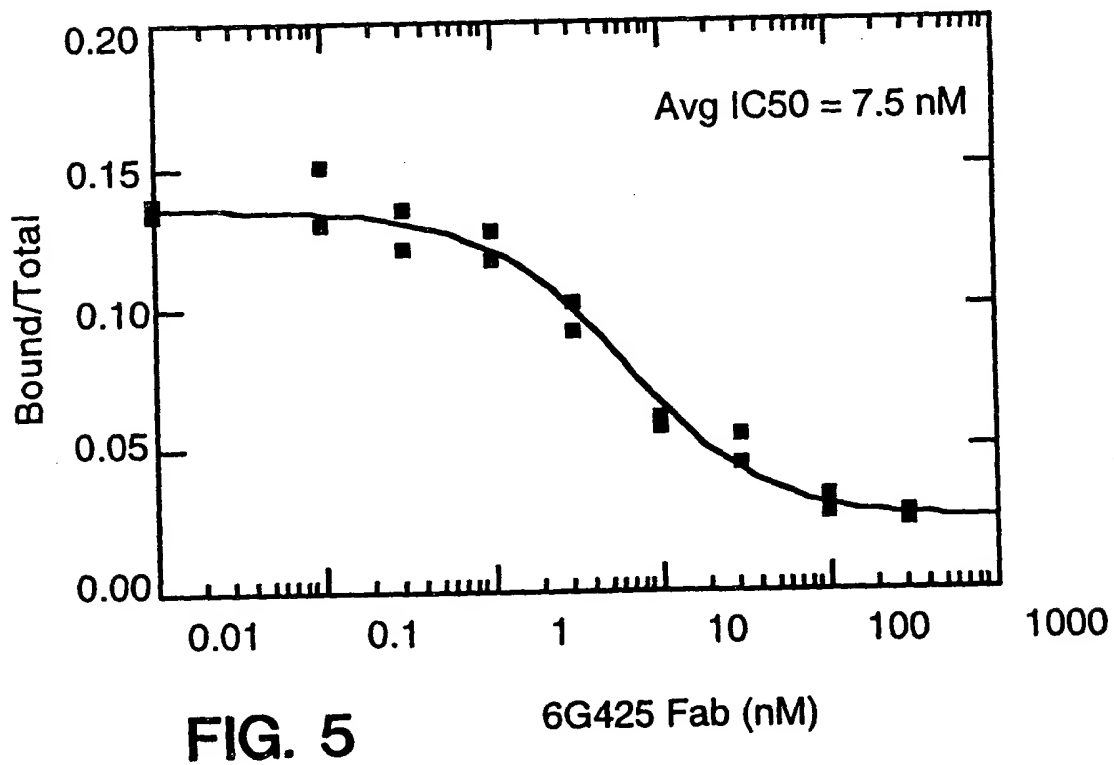
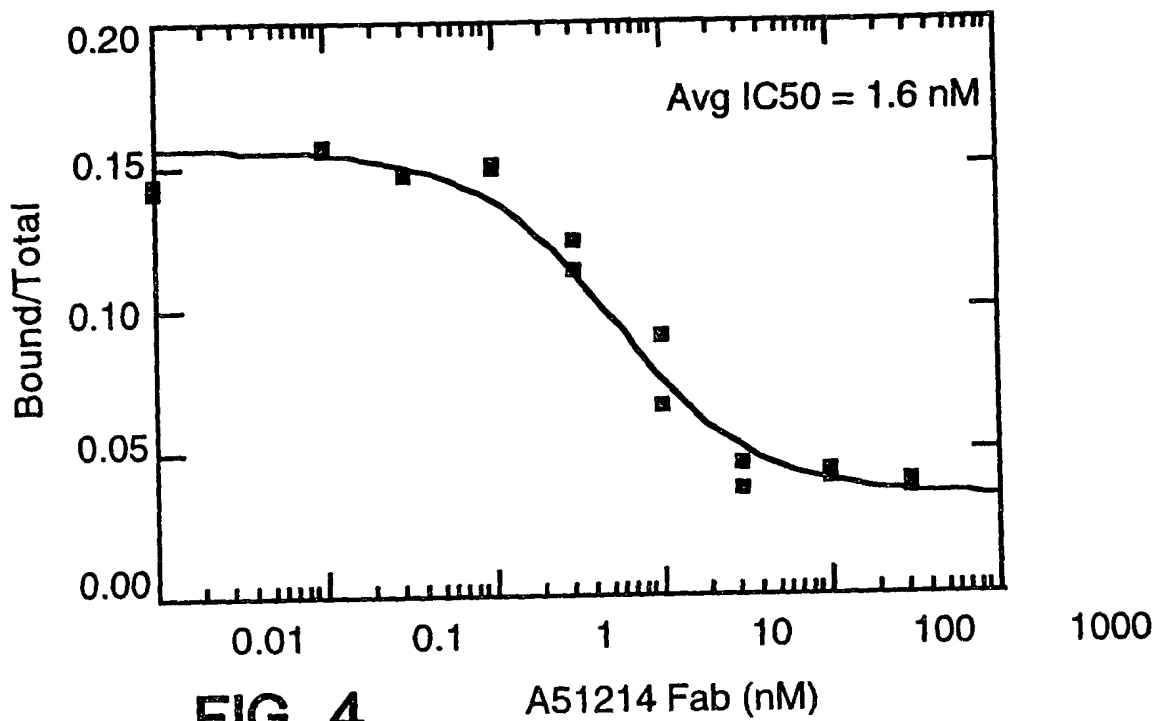


FIG. 1







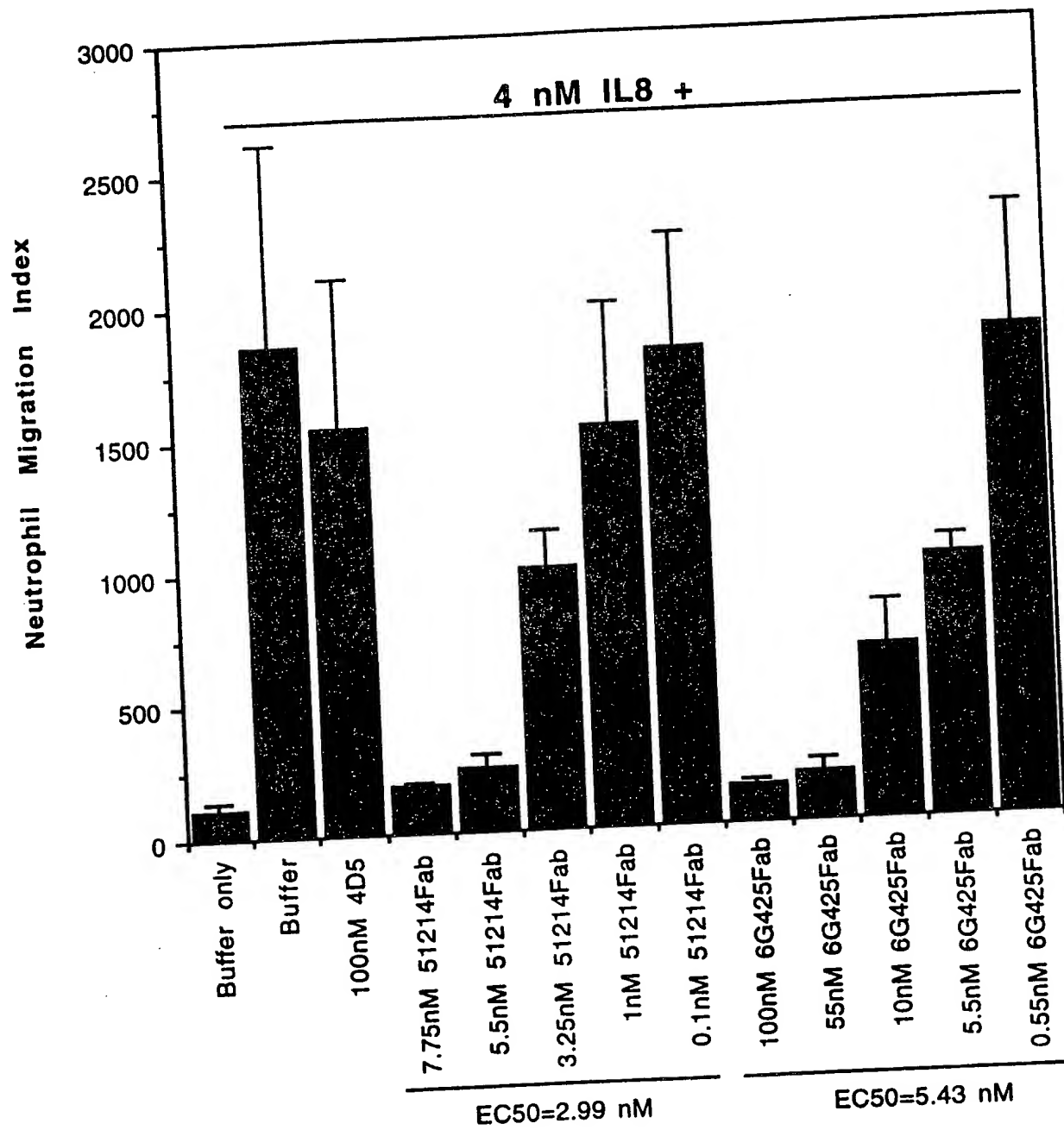


FIG. 6

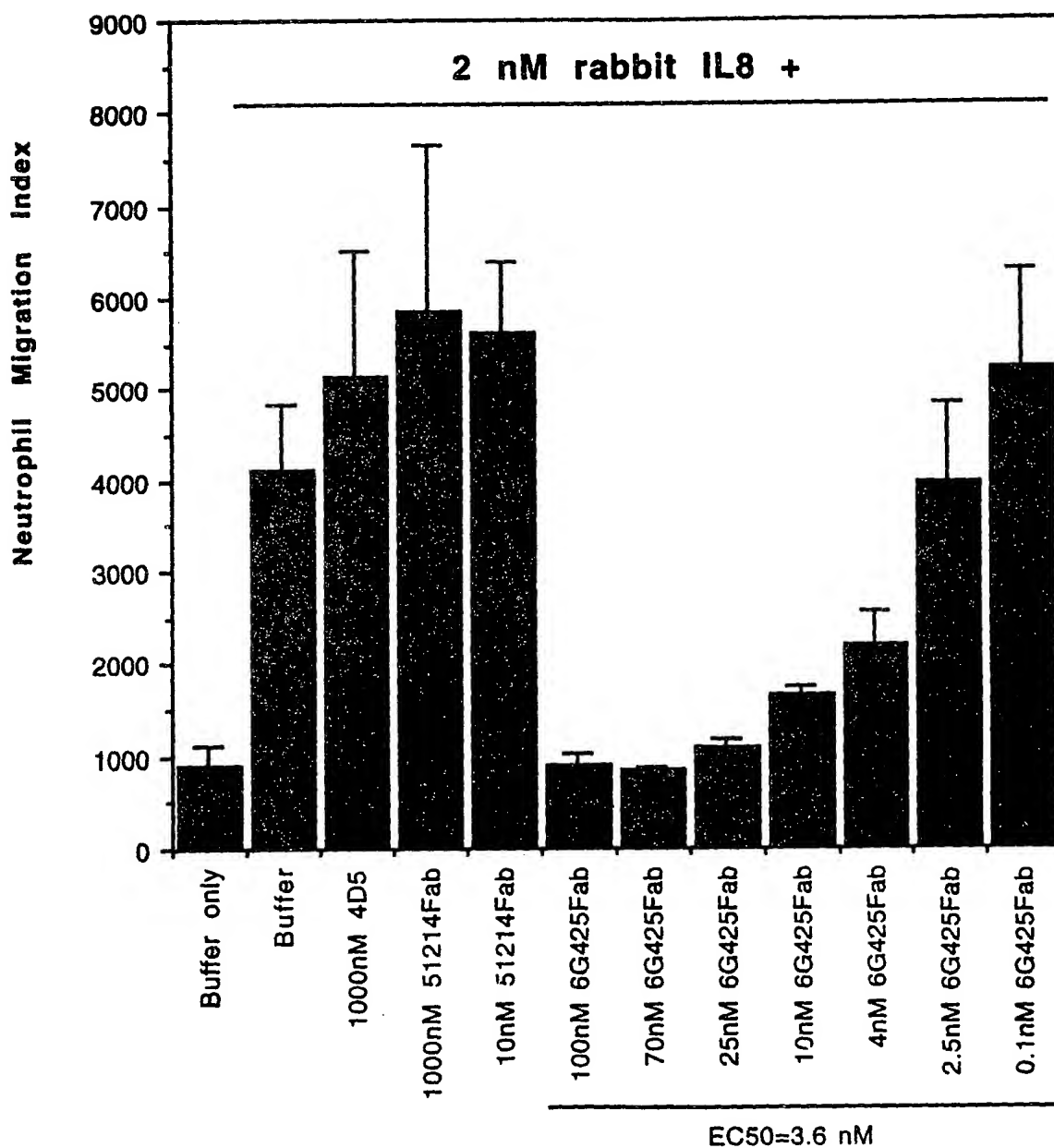


FIG. 8

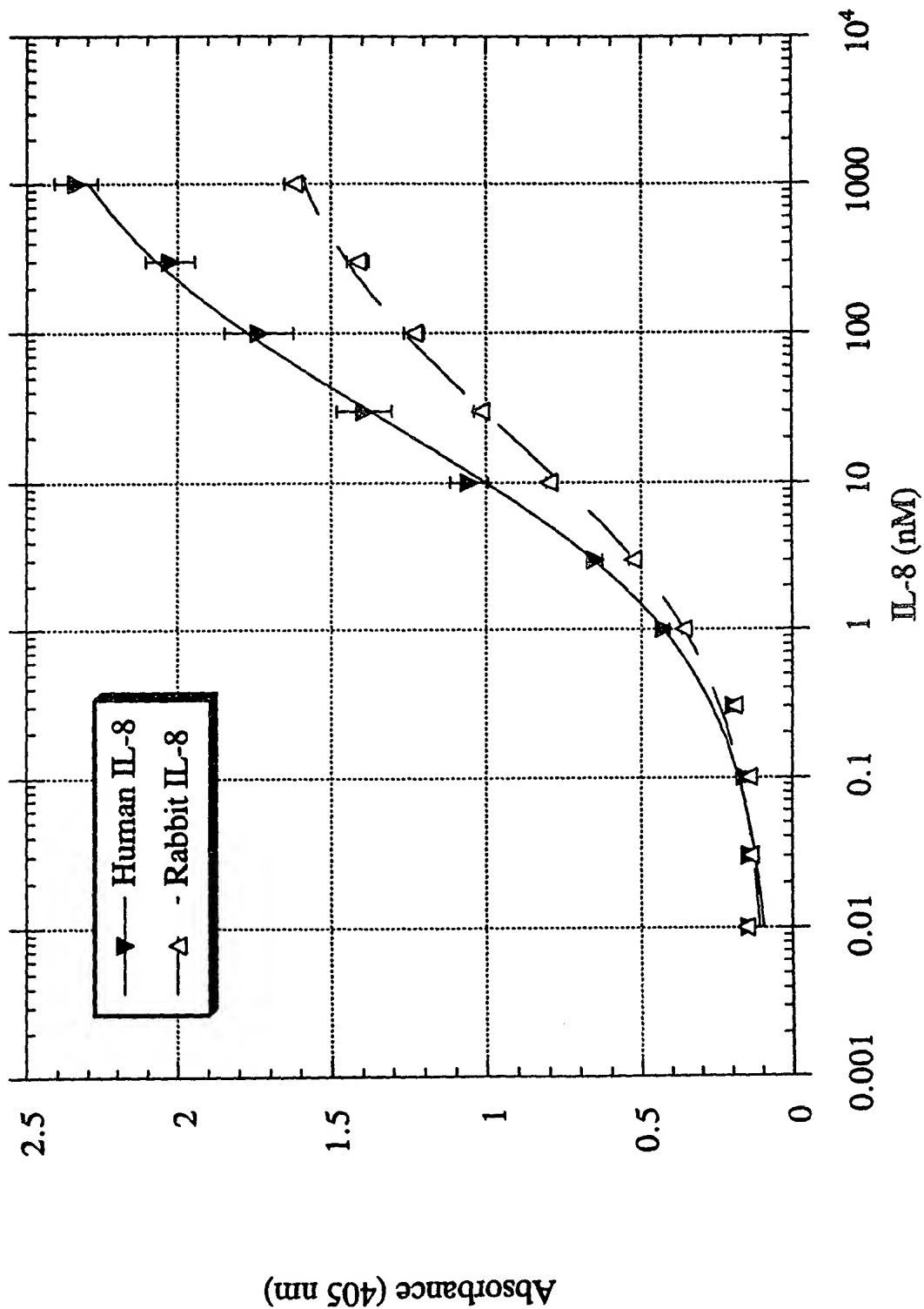


FIG. 9

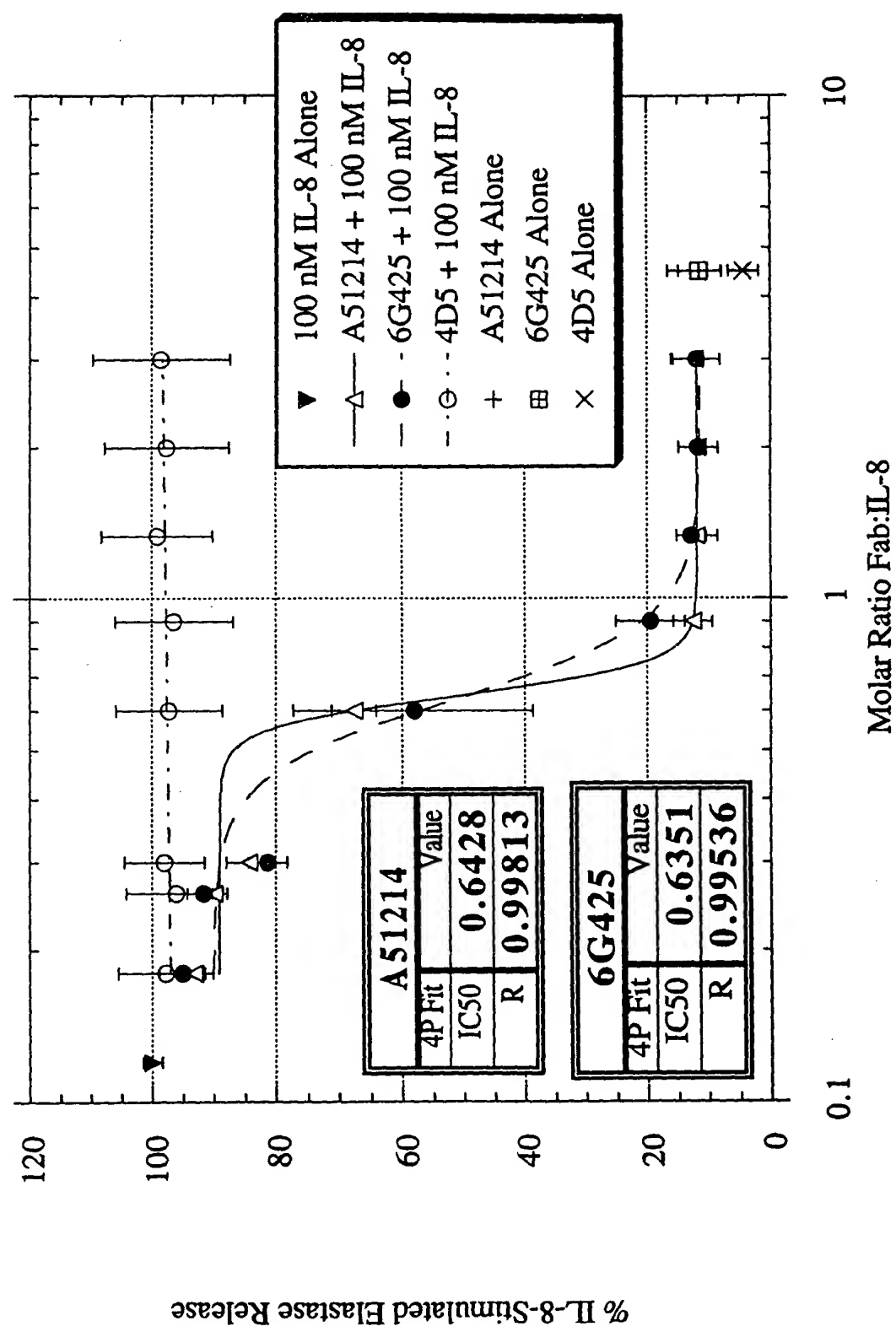
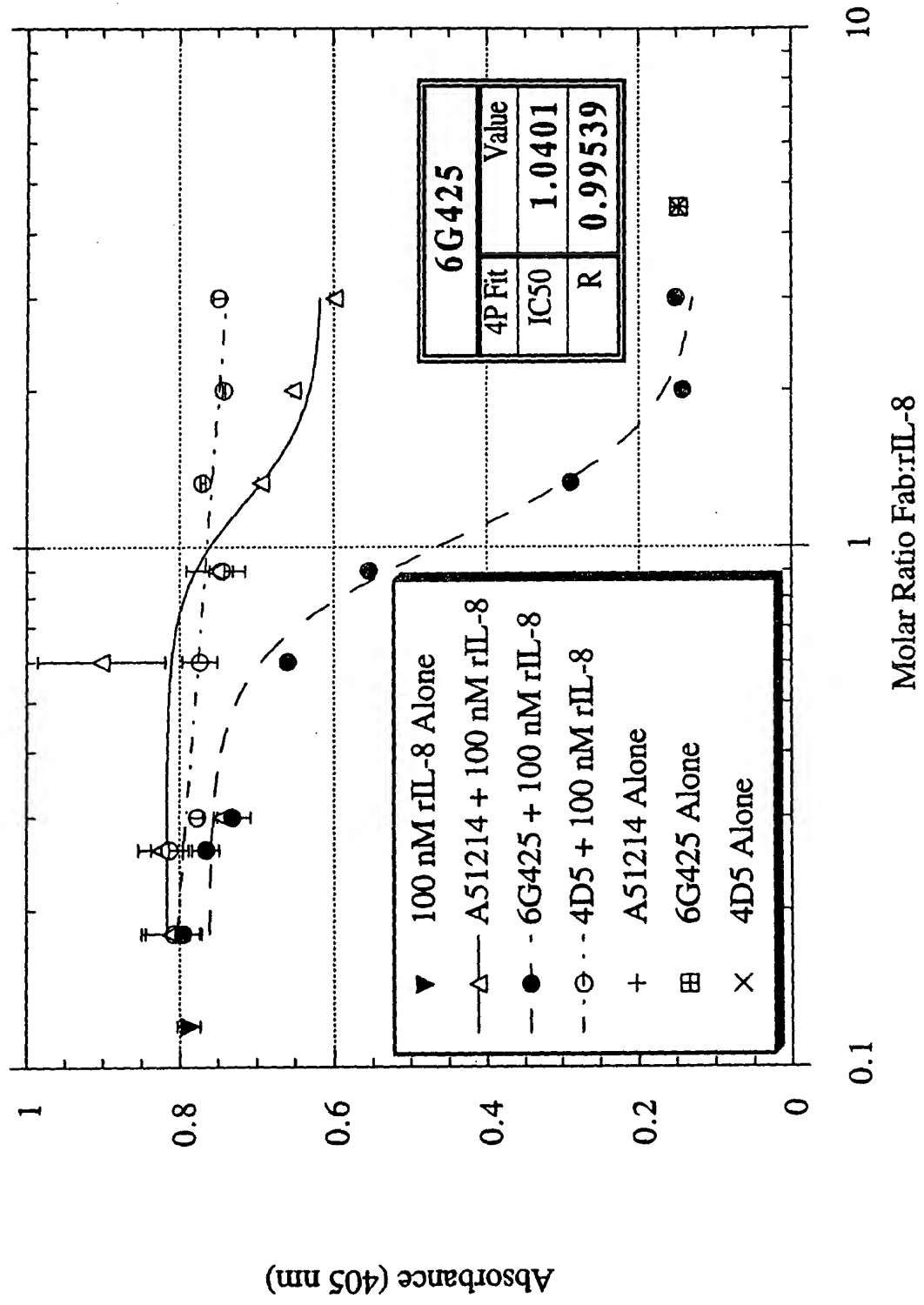


FIG. 10



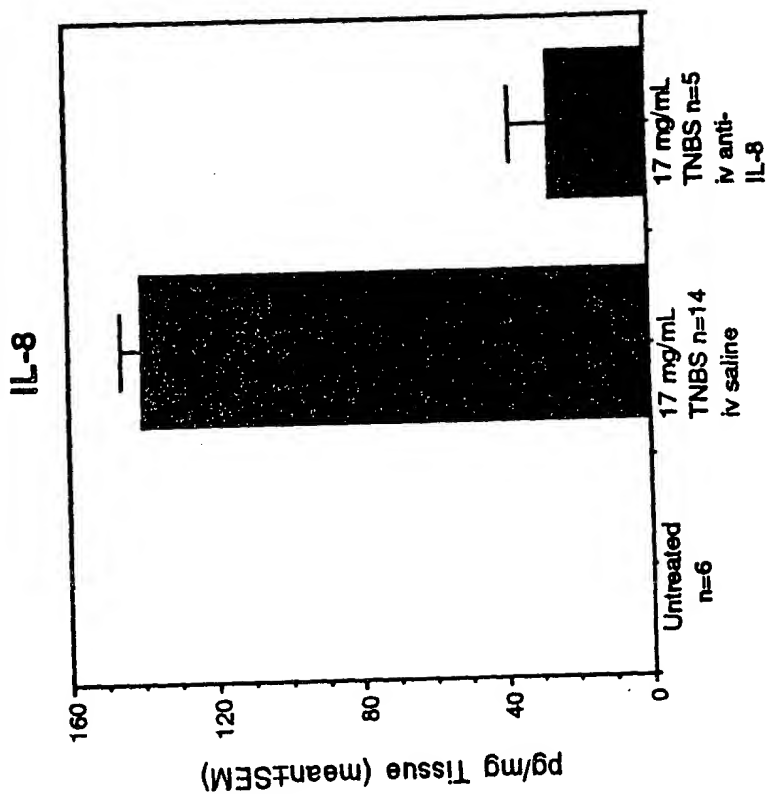


FIG. 11B

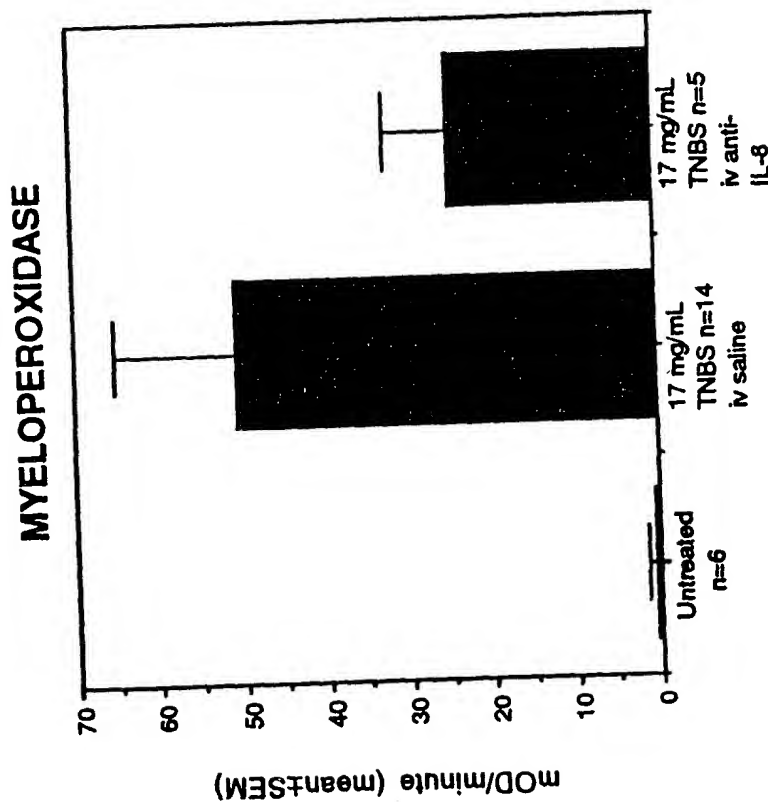


FIG. 11A

TOP SECRET

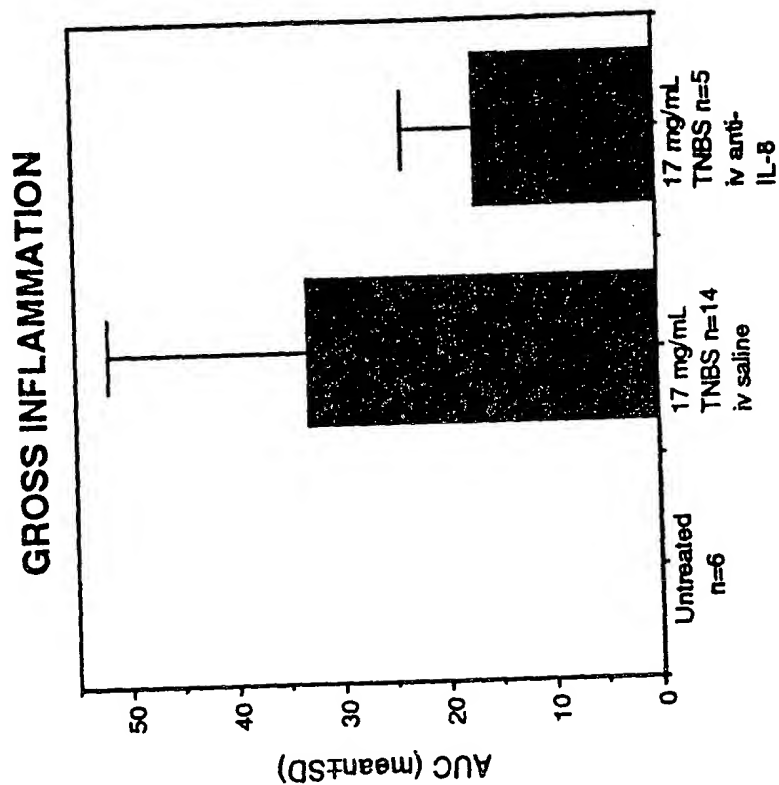


FIG. 11D

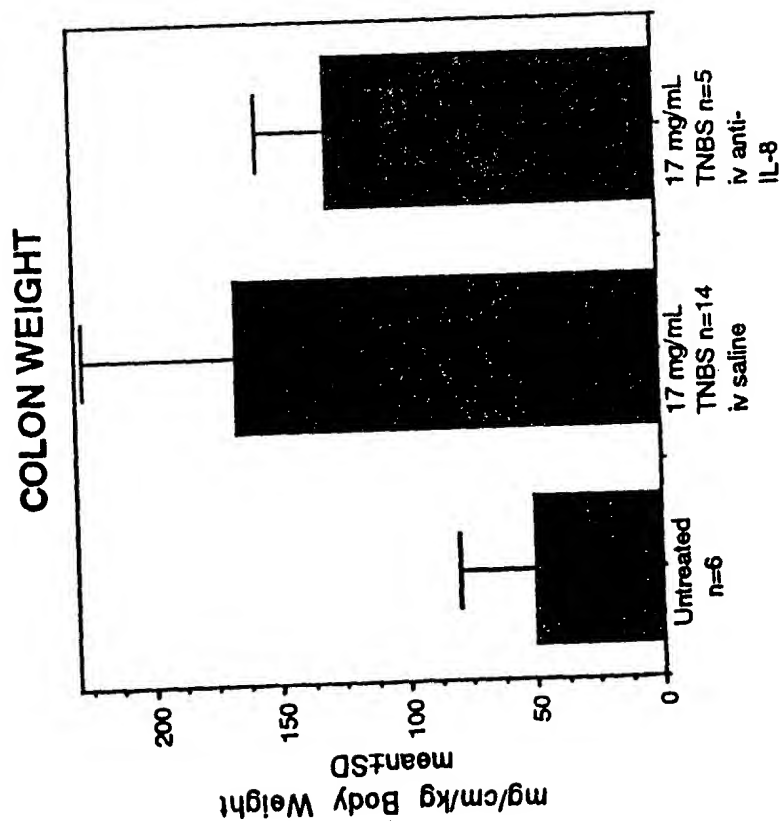


FIG. 11C

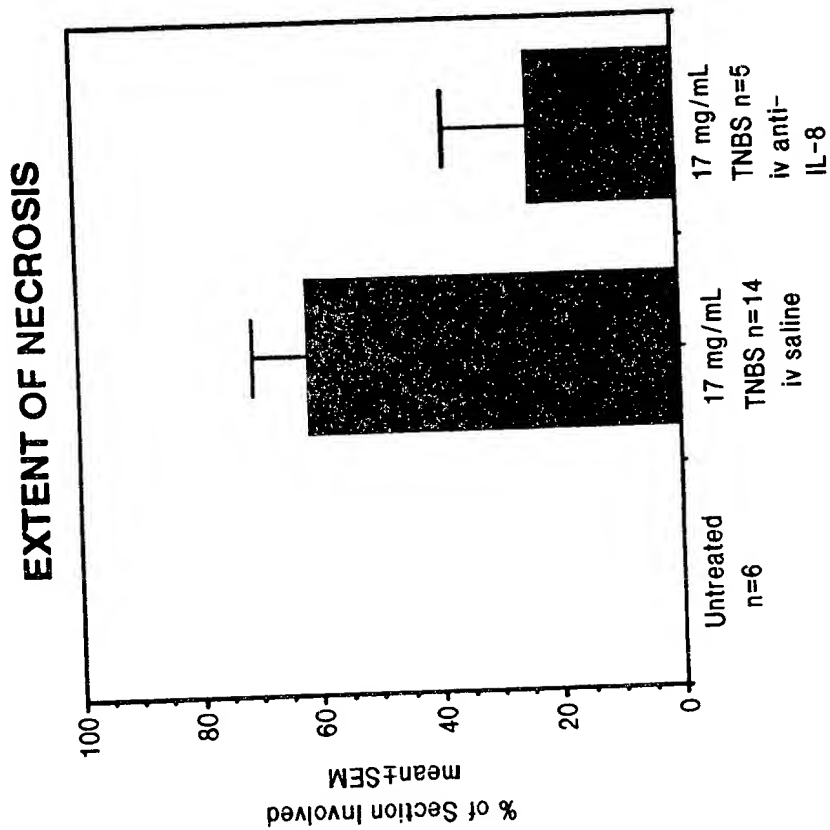


FIG. 11F

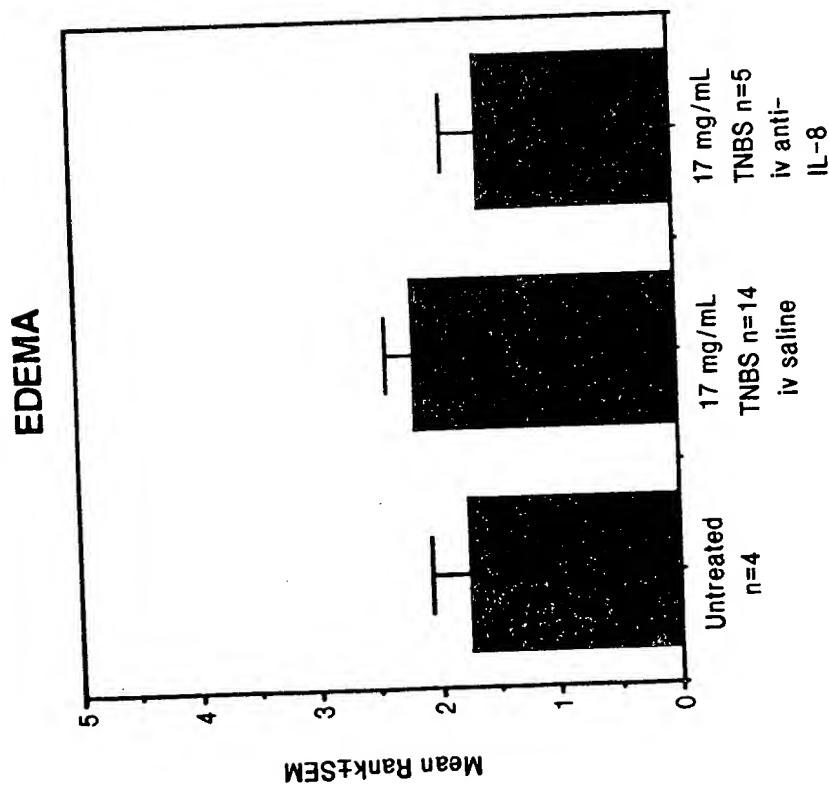


FIG. 11E

TOP SECRET 60

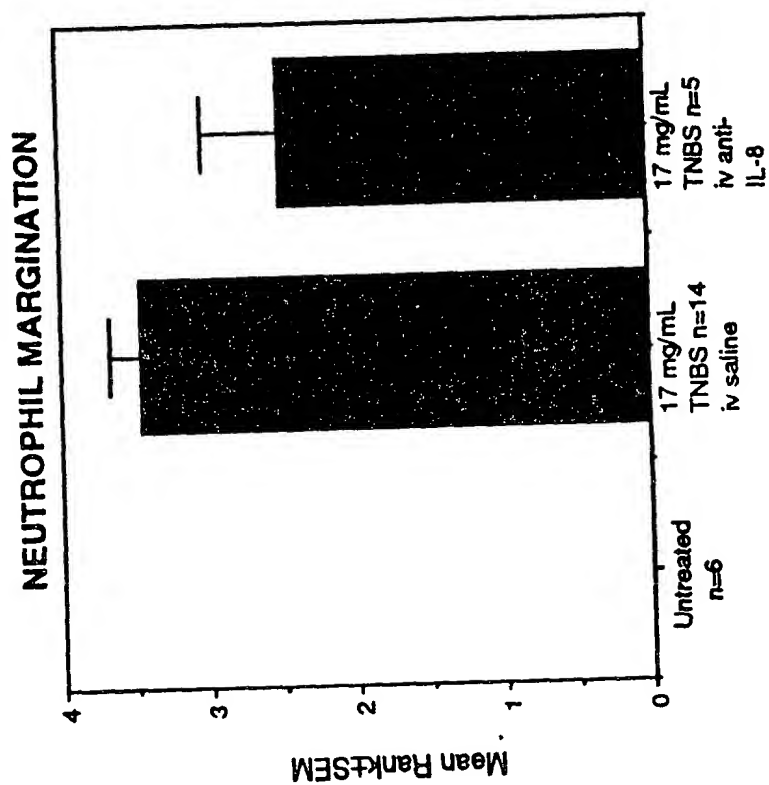


FIG. 11H

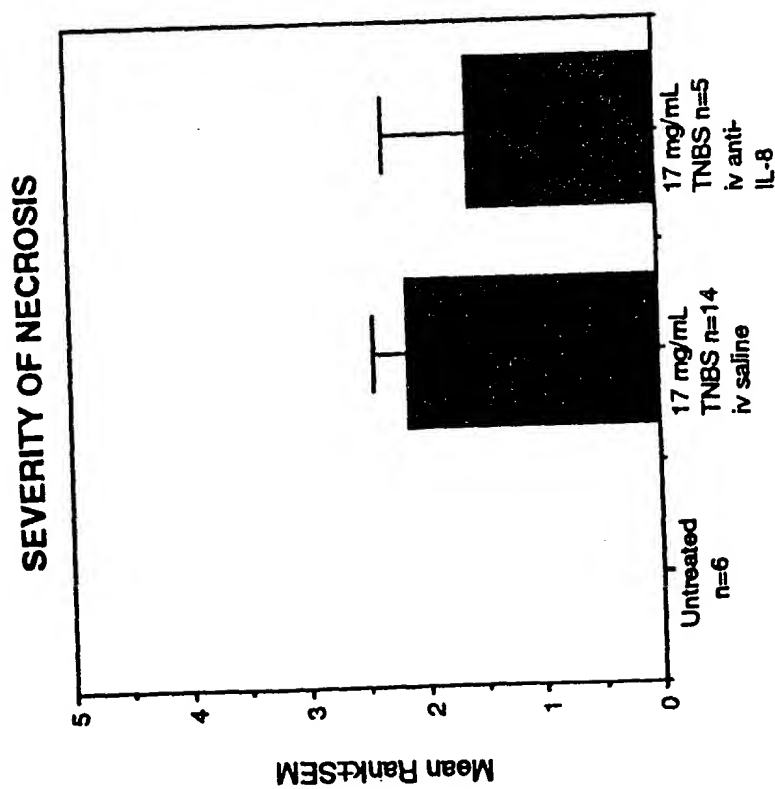


FIG. 11G

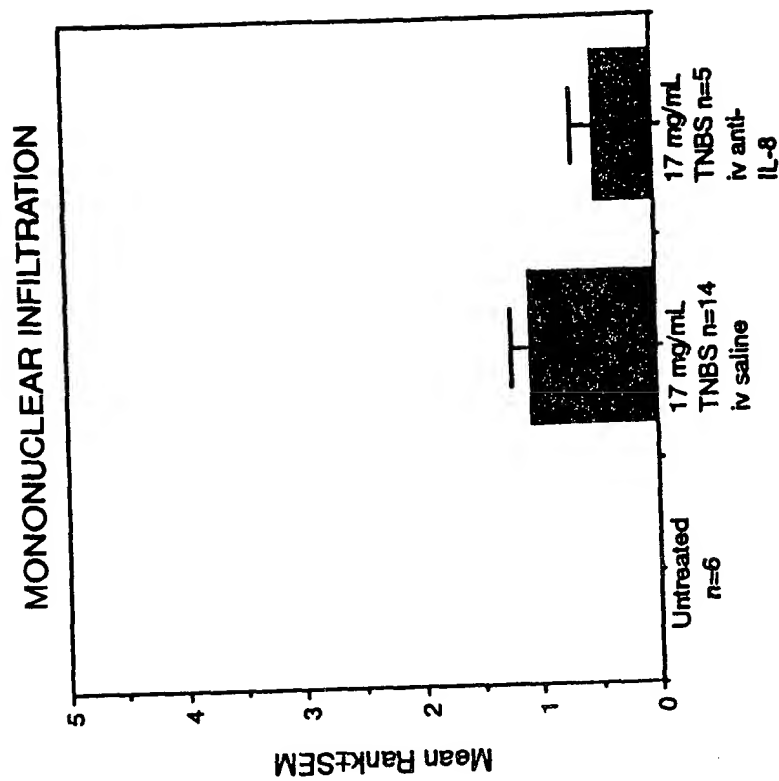


FIG. 11J

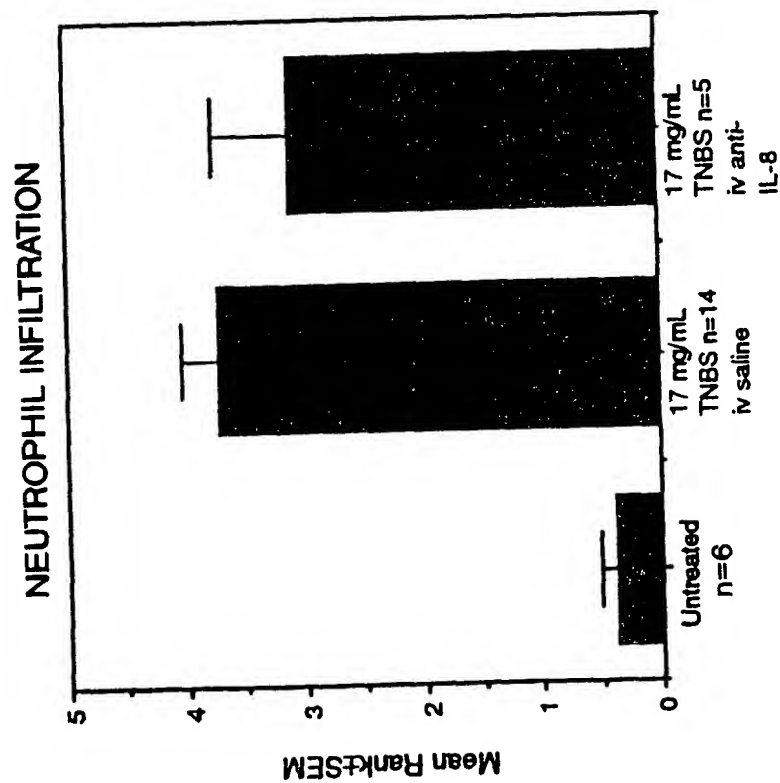
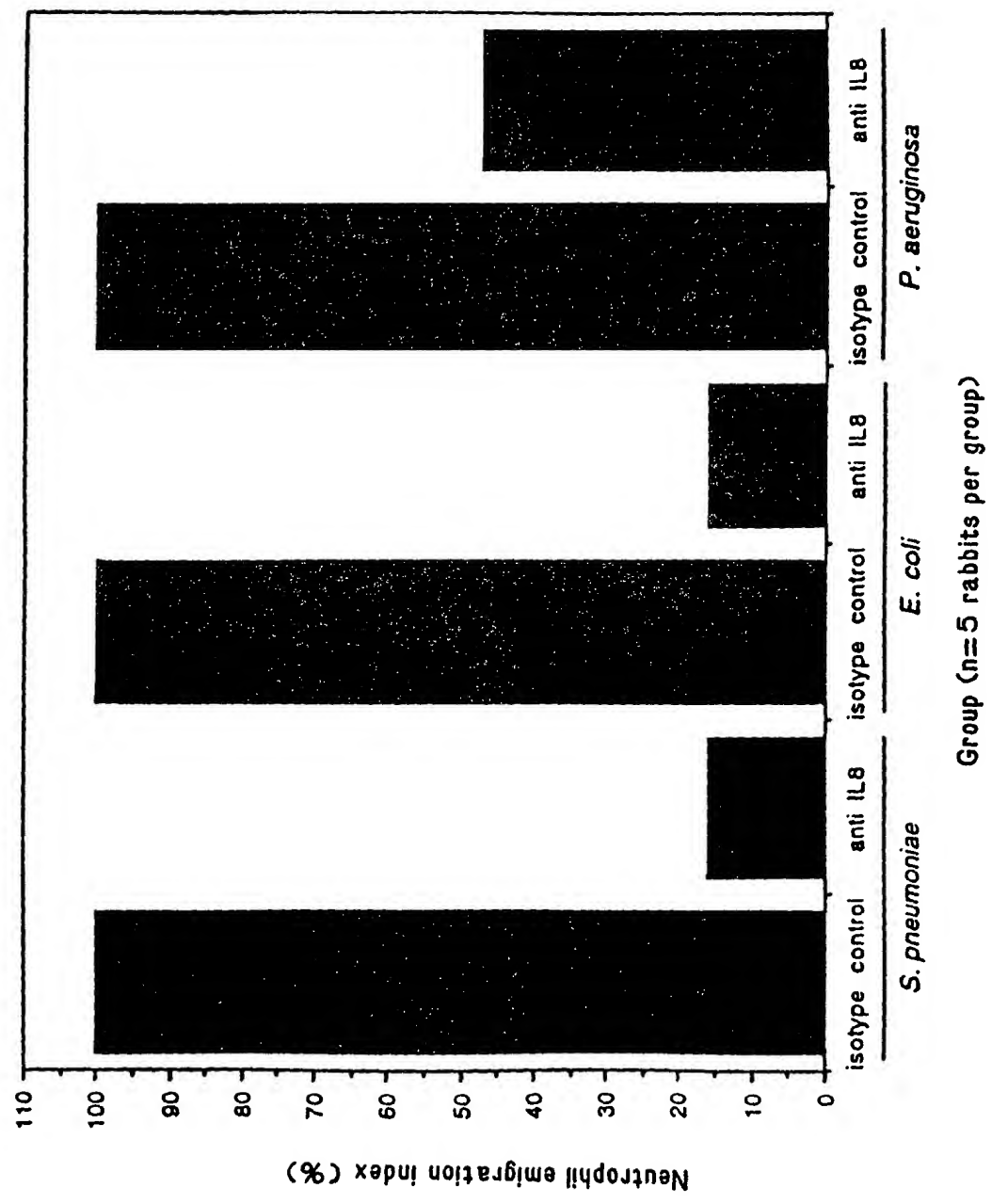


FIG. 11I

FIG. 12



Light Chain Primers:

FIG. 13

MKLC-1, 22mer

5' CAGTCCAACGTGTCAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3' (SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3' (SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3' (SEQ ID NO.4)

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3' (SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)

FIG. 14

Light chain forward primer

SL001A-2 35 mer

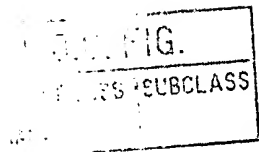
5' ACAACGCGTACGCT GACATCGTCATGACCCAGTC 3' (SEQ ID NO.7)
T T (SEQ ID NO.8)
A (SEQ ID NO.9)

Light chain reverse primer

SL001B 37 mer

5' GCTCTTCGAATG GTGGGAAGATGGATACAGTTGGTGC 3' (SEQ ID NO.10)

TOP SECRET



Heavy chain forward primer SL002B 39 mer 5' CGATGGGCCCGG ATAGACCGATGGGGCTGTGTTTGGC 3' (SEQ ID NO.11) T (SEQ ID NO.12) G (SEQ ID NO.13) A (SEQ ID NO.14)

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCGG ATAGACCGATGGGGCTGTGTTTGGC 3' (SEQ ID NO.11)
T (SEQ ID NO.15)
A (SEQ ID NO.14)
G (SEQ ID NO.13)

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCGG ATAGACCGATGGGGCTGTGTTTGGC 3' (SEQ ID NO.11)
T (SEQ ID NO.15)
A (SEQ ID NO.14)
G (SEQ ID NO.13)

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCGG ATAGACCGATGGGGCTGTGTTTGGC 3' (SEQ ID NO.11)
T (SEQ ID NO.15)
A (SEQ ID NO.14)
G (SEQ ID NO.13)

1 GACATTGTCA TGACACAGTC TCATAAATTC ATGTCCACAT CAGTAGGAGA CAGGTCAGC
CTGTAACAGT ACTGTGTCAG AGTTTAAAG TACAGGTGTA GTCATCCTCT GTCCCAGTCG
1 D I V M T Q S Q K F M S T S V G D R V S

61 GTCACCTGCA AGGCCAGTCA GAATGTGGT ACTAATGTAG CCTGGTATCA ACAGAAACCA
CAGTGGACGT TCCGGTCAGT CTTACACCCA TGATTACATC GGACCATAGT TGCTTTGGT
21 V T C K A S Q N V G T N V A W Y Q Q K P
* * * * * * * * * * * * * * *

CDR #1

121 GGGCAATCTC CTAAGCACT GATTACTCG TCATCCTACC GGTACAGTGG AGTCCCTGAT
CCCGTTAGAG GATTTCGTGA CTAATGAGC AGTAGGATGG CCATGTCACC TCAGGGACTA
41 G Q S P K A L I Y S S Y R Y S G V P D
* * * * * * * * * * * * * *

CDR #2

181 CGCTTCACAG GCAGTGGATC TGGACAGAT TTCACTCTCA CCATCAGCCA TGTGCAGTCT
GGAAAGTGTG CGTCACCTAG ACCCTGTCTA AAGTGAGAGT GGATGTCGGT ACACGTCAGA
61 R F T G S G S G T D F T L T I S H V Q S

241 GAAGACTTGG CAGACTATT CTGTCAGCAA TATAACATCT ATCCTCTCAC GTTCGGTCTT
CTTCTGAACC GTCTGATAAA GACAGTCGTT ATATTGTAGA TAGGAGAGTG CAAGCCAGGA
81 E D L A D Y F C Q Q Y N I Y P L T F G P
* * * * * * * * * * * * * *

CDR #3

301 GGGACCAAGC TGGAGTTGAA ACGGGCTGAT GCTGCACCAC CAACTGTATC CATCTTCCCA
CCCTGGTTCG ACCTCAACTT TGCCCGACTA CGACGTGGTG GTTGACATAG GTAGAAGGGT
101 G T K L E L K R A D A A P P T V S I F P

BstBI

361 CCAATTCGAA (SEQ ID NO.16)
GGTAAGCTT (SEQ ID NO.17)
121 P F E

FIG. 16

1 TTCTATTGCT ACAAACGCGT ACGCTGAGGT GCAGCTGGTG GAGTCTGGGG GAGGCTTAGT
AAGATAACGA TGTTTGCGCA TGCGACTCCA CGTCGACCAC CTCAGACCCC CTCCGAATCA
1 E V Q L V E S G G G L V

61 GCCGCCTGGA GGGTCCCTGA AACTCTCCTG TGCAGCCTCT GGATTCATAT TCAGTAGTTA
CGGCGGACCT CCCAGGGACT TTGAGAGGAC ACGTCGGAGA CCTAAGTATA AGTCATCAAT
13 P P G G S L K L S C A A S G F I F S S Y
* *

CDR #1

121 TGGCATGTCT TGGGTTCGCC AGACTCCAGG CAAGAGCCTG GAGTTGGTCG CAACCATTAA
ACCGTACAGA ACCCAAGCGG TCTGAGGTCC GTTCTCGGAC CTCAACCAGC GTTGGTAATT
33 G M S W V R Q T P G K S L E L V A T I N
* * * * *

181 TAATAATGGT GATAGCACCT ATTATCCAGA CAGTGTGAAG GGCCGATTCA CCATCTCCCG
ATTATTACCA CTATCGTGGA TAATAGGTCT GTCACACTTC CCGGCTAAGT GGTAGAGGGC
53 N N G D S T Y Y P D S V K G R F T I S R
* * * * *

CDR #2

241 AGACAATGCC AAGAACACCC TGTACCTGCA AATGAGCAGT CTGAAGTCTG AGGACACAGC
TCTGTTACCG TTCTTGTTGGG ACATGGACGT TTA CTGCTCA GACTTCAGAC TCCTGTGTCTG
73 D N A K N T L Y L Q M S S L K S E D T A

301 CATGTTTTAC TGTGCAAGAG CCCTCATTAG TTCGGCTACT TGGTTTGGTT ACTGGGGCCA
GTACAAAATG ACACGTTCTC GGGAGTAATC AAGCCGATGA ACCAAACCAA TGACCCCGGT
93 M F Y C A R A L I S S A T W F G Y W G Q
* * * * *

CDR #3

361 AGGGACTCTG GTCAGTGTCT CTGCAGCCAA AACAACAGCC CCATCTGTCT
TCCCTGAGAC CAGTGACAGA GACGTCGGTT TTGTTGTCTG GGTAGACAGA
113 G T L V T V S A A K T T A P S V Y

ApaI

411 ATCCGGG (SEQ ID NO.18)
TAGGCC (SEQ ID NO.19)
130 P

FIG. 17

FIG. 18

VL.front 31-MER

5' ACAAACGCGTACGCTGATATCGTCATGACAG 3' (SEQ ID NO.20)

VL.rear 31-MER

5' GCAGCATCAGCTCTTCGAAGCTCCAGCTTGG 3' (SEQ ID NO.21)

VH.front.SPE 21-MER

5' CCACTAGTACGCAAGTTCACG 3' (SEQ ID NO.22)

VH.rear 33-MER

5' GATGGGCCCTTG GTGGAGGCTGCAGAGACAGTG 3' (SEQ ID NO.23)

1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG ATATCGTCAT GACACAGTCT CAAAAATTCA TGTCCACATC AGTAGGAGAC
CGCATGCGAC TATAGCAGTA CTGTGTGAGA GTTTTAAAGT ACAGGTGTAG TCATCCTCTG
-3 A Y A D I V M T Q S Q K F M S T S V G D

121 AGGGTCAGCG TCACCTGCAA GGCCAGTCAG AATGTGGGTA CTAATGTAGC CTGGTATCAA
TCCAGTCGC AGTGGACGTT CCGGTGAGTC TTACACCCAT GATTACATCG GACCATAGTT
18 R V S V T C K A S O N V G T N V A W Y Q
* * * * *

CDR #1

181 CAGAAACCAG GGCAATCTCC TAAAGCACTG ATTTACTCGT CATCCTACCG GTACAGTGGA
GTCTTTGGTC CCGTTAGAGG ATTTCTGTGAC TAAATGAGCA GTAGGATGGC CATGTACCT
38 Q K P G Q S P K A L I Y S S S Y R Y S G
* * * * *

CDR #2

241 GTCCCTGATC GCTTCACAGG CAGTGGATCT GGGACAGATT TCACTCTCAC CATCAGCCAT
CAGGGACTAG CGAAGTGTCC GTCACCTAGA CCCTGTCTAA AGTGAGAGTG GTAGTCGGTA
58 V P D R F T G S G S G T D F T L T I S H

301 GTGCAGTCTG AAGACTTGGC AGACTATTTT TGTGAGCAAT ATAACATCTA TCCTCTCACG
CACGTCAGAC TTCTGAACCG TCTGATAAAG ACAGTCGTTA TATTGTAGAT AGGAGAGTGC
78 V Q S E D L A D Y F C Q Q Y N I Y P L T
* * * * *

CDR #3

BstBI

361 TTCGGTCCTG GGACCAAGCT GGAGCTTTCGA AGAGCTGTGG CTGCACCATC TGTCTTCATC
AAGCCAGGAC CCTGGTTCGA CCTCGAAGCT TCTCGACACC GACGTGGTAG ACAGAAGTAG
98 F G P G T K L E L R R A V A A P S V F I

421 TTCCCGCCAT CTGATGAGCA GTTGAAATCT GGAAGTGGCT CTGTTGTGTG CCTGCTGAAT
AAGGGCGGTA GACTACTCGT CAACTTTAGA CCTTGACGAA GACAACACAC GGACGACTTA
118 F P P S D E Q L K S G T A S V V C L L N

481 AACTTCTATC CCAGAGAGGC CAAAGTACAG TGGAAGGTGG ATAACGCCCT CCAATCGGGT
TTGAAGATAG GGTCTCTCCG GTTTCATGTC ACCTTCCACC TATTGCGGGA GGTAGCCCA
138 N F Y P R E A K V Q W K V D N A L Q S G

541 AACTCCCAGG AGAGTGTAC AGAGCAGGAC AGCAAGGACA GCACCTACAG CCTCAGCAGC
TTGAGGGTCC TCTCACAGTG TCTCGTCCTG TCGTTCCTGT CGTGGATGTC GGAGTCGTG
158 N S Q E S V T E Q D S K D S T Y S L S S

601 ACCCTGACGC TGAGCAAAGC AGACTACGAG AAACACAAAG TCTACGCCTG CGAAGTCACC
TGGGACTGCG ACTCGTTTCG TCTGATGCTC TTTGTGTTTC AGATGCGGAC GCTTCAGTGG
178 T L T L S K A D Y E K H K V Y A C E V T

661 CATCAGGGCC TGAGCTCGCC CGTCACAAAG AGCTTCAACA GGGGAGAGTG
GTAGTCCCGG ACTCGAGCGG GCAGTGTTC TCGAAGTTGT CCCCTCTCAC
198 H Q G L S S P V T K S F N R G E C (SEQ ID NO.25)

711 TTAA (SEQ ID NO.24)
AATT
216 O

FIG. 19

09736338-033101

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCTG TTTTCTCTAT TGCTACAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGGTGCAGCT GGTGGAGTCT GGGGGAGGCT TAGTGCCGCC TGGAGGGTCC
CGCATGCGAC TCCACGTCTGA CCACCTCAGA CCCCCTCCGA ATCACGGCGG ACCTCCCAGG
-3 A Y A E V Q L V E S G G G L V P P G G S

121 CTGAAACTCT CCTGTGCAGC CTCTGGATTC ATATTCAGTA GTTATGGCAT GTCTTGGGTT
GACTTTGAGA GGACACGTCG GAGACCTAAG TATAAGTCAT CAATACCGTA CAGAACCCAA
18 L K L S C A A S G F I F S S Y G M S W V
* * * *

CDR #1

181 CGCCAGACTC CAGGCAAGAG CCTGGAGTTG GTCGCAACCA TTAATAATAA TGGTGATAGC
GCGGTCTGAG GTCCGTTCTC GGACCTCAAC CAGCGTTGGT AATTATTATT ACCACTATCG
38 R Q T P G K S L E L V A T I N N N G D S
* * * * *

241 ACCTATTATC CAGACAGTGT GAAGGGCCGA TTCACCATCT CCCGAGACAA TGCCAAGAAC
TGGATAATAG GTCTGTCACA CTTCCCGGCT AAGTGGTAGA GGGCTCTGTT ACGGTTCTTG
58 T Y Y P D S V K G R F T I S R D N A K N
* * * * *

CDR #2

301 ACCCTGTACC TGCAAATGAG CAGTCTGAAG TCTGAGGACA CAGCCATGTT TTAGTGTGCA
TGGGACATGG ACGTTTACTC GTCAGACTTC AGACTCCTGT GTCGGTACAA AATGACACGT
78 T L Y L Q M S S L K S E D T A M F Y C A
361 AGAGCCCTCA TTAGTTCGGC TACTTGGTTT GGTTACTGGG GCCAAGGGAC TCTGGTCACT
TCTCGGGAGT AATCAAGCCG ATGAACCAAA CCAATGACCC CGGTTCCCTG AGACCAGTGA
98 R A L I S S A T W F G Y W G Q G T L V T
* * * * *

CDR #3

ApaI

421 GTCTCTGCAG CCTCCACCAA GGGCCCATCG GTCTTCCCCC TGGCACCCCTC CTCCAAGAGC
CAGAGACGTC GGAGGTGGTT CCCGGGTAGC CAGAAGGGGG ACCGTGGGAG GAGGTTCTCG
118 V S A A S T K G P S V F P L A P S S K S

481 ACCTCTGGGG GCACAGCGGC CCTGGGCTGC CTGGTCAAGG ACTACTTCCC CGAACCGGTG
TGGAGACCCC CGTGTGCGCCG GGACCCGACG GACCAGTTCC TGATGAAGGG GCTTGGCCAC
138 T S G G T A A L G C L V K D Y F P E P V

541 ACGGTGTCGT GGAACCTCAGG CGCCCTGACC AGCGGCGTGC ACACCTTCCC GGCTGTCCTA
TGCCACAGCA CCTTGAGTCC GCGGGACTGG TCGCCGCACG TGTGGAAGGG CCGACAGGAT
158 T V S W N S G A L T S G V H T F P A V L

601 CAGTCCTCAG GACTCTACTC CCTCAGCAGC GTGGTGACCG TGCCCTCCAG CAGCTTGGGC
GTCAGGAGTC CTGAGATGAG GGAGTCGTCG CACCACTGGC ACGGGAGGTC GTCGAACCCG
178 Q S S G L Y S L S S V V T V P S S S L G

FIG. 20A

661 ACCCAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAAA
 TGGGTCTGGA TGTAAGACGTT GCACTTAGTG TTCGGGTCGT TGTGGTTCCA CCTGTTCTTT
 198 T Q T Y I C N V N H K P S N T K V D K K
 721 GTTGAGCCCA AATCTTGTGA CAAACTCAC ACATGA (SEQ ID NO.26)
 CAACTCGGT TTAGAACACT GTTTTGAGTG TGTACT
 218 V E P K S C D K T H T O (SEQ ID NO.27)

FIG. 20B

Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCAACGTGTCAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3' (SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3' (SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3' (SEQ ID NO.4)

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3' (SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)

FIG. 21

TOP SECRET "SECRET" 2260

FIG.	
SUBCLASS	

Light chain forward primer

6G4.light.Nsi 36-MER

5' CCAATGCATACGCT GAC ATC GTG ATG ACC CAG ACC CC 3' (SEQ ID NO.28)
T T T A A
(SEQ ID NO.29)
(SEQ ID NO.30)

Light chain reverse primer

6G4.light.Mun 35-MER

5' AGA TGT CAA TTG CTC ACT GGA TGG TGG GAA GAT GG 3' (SEQ ID NO.31)

FIG. 22

Heavy chain forward primer

6G4.heavy.Mlu 32-MER

5' CAAACGCGTACGCT GAG ATC CAG CTG CAG CAG 3' (SEQ ID NO.32)
T C (SEQ ID NO.33)

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCGG ATAGACCGATGGGGCTGTTGTTTGGC 3' (SEQ ID NO.11)
T A G (SEQ ID NO.15)
(SEQ ID NO.14)
(SEQ ID NO.13)

FIG. 23

70 G ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT
C TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA
1 D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGCAG ATCTAGTCAG AGCCTTGTAC ACGGTATTGG AAACACCTAT
GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA
18 Q A S I S C R S S O S L V H G I G N T Y
* * * * *

CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
AATGTAACCA TGGACGTCTT CGGTCCGGTC AGAGGTTTTCG AGGACTAGAT GTTTCAAAGG
38 L H W Y L Q K P G Q S P K L L I Y K V S
* * * * *

CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTC AGTGGCAGTG GATCAGGGAC AGATTTTCACA
TTGGCTAAAA GACCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
58 N R F S G V P D R F S G S G S G T D F T
* * * *

301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT
78 L R I S R V E A E D L G L Y F C S Q S T
* * * *

CDR #3

361 CATGTTCCGC TCACGTTCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGATGCTGCA
GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCC ACTACGACGT
98 H V P L T F G A G T K L E L K R A D A A
* * * *

MunI

421 CCAACTGTAT CCATCTTCCC ACCATCCAGT GAGCAATTGA (SEQ ID NO.34)
GGTTGACATA GGTAGAAGGG TGGTAGGTCA CTCGTTAACT
118 P T V S I F P P S S E Q L K (SEQ ID NO.35)

FIG. 24

70 G AGATTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
C TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
1 E I Q L Q Q S G P E L M K P G A S
121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTCAGTA GCCACTACAT GCACTGGGTG
CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
18 V K I S C K A S G Y S F S S H Y M H W V
* * * *

CDR #1

181 AAGCAGAGCC ATGGAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
TTCGTCTCGG TACCTTTCTC GGAAGTCACC TAACCGATGT AACTAGGAAG GTTACCACTT
38 K Q S H G K S L E W I G Y I D P S N G E
* * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAAGT GACATCTGTG TAGAAGGTGC
58 T T Y N Q K F K G K A T L T V D T S S S
* * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
TCTCCCTGA TATCTATGTT GCCGCTGACC AAAAAGCTAC AGACCCCGCG TCCCTGGTGC
98 R G D Y R Y N G D W F F D V W G A G T T
* * * * *

CDR #3

BstEII ApaI
421 GTCACCGTCT CCTCCGCCAA AACCAGACAGC CCCATCGGTC TATCCGGGCC
CAGTGGCAGA GGAGGCGGAT TTGGCTGTCG GGGTAGCCAG ATAGGCCCGG
118 V T V S S A K T D S P I G L S G P

471 CATC (SEQ ID NO.36)
GTAG
135 I (SEQ ID NO.37)

FIG. 25

FIG.

SUBCLASS

5' CTTGGTGGAGGCGGAGGAGACG 3' (SEQ ID NO.38)

Mutagenesis Primer for 6G425VL

DS/VF 38MER

5' GAAACGGGCTGTTGCTGCACCAACTGTATTCATCTTCC 3' (SEQ ID NO.39)

SYN.BstEII 31 MER

5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3' (SEQ ID NO.40)

SYN.Apa 22 MER

5' CTTGGTGGAGGCGGAGGAGACG 3' (SEQ ID NO.38)

FIG. 26

1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAT
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTA
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGAGAGT
CGTATGCGAC TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA
-3 A Y A D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGCAAG ATCTAGTCAG AGCCTTGTCAC ACGGTATTGG AAACACCTAT
GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA
18 Q A S I S C R S S O S L V H G I G N T Y
* * * * * * * * * * * * *

CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
AATGTAACCA TGGACGTCTT CGGTCCGGTC AGAGGTTTTCG AGGACTAGAT GTTTCAAAGG
38 L H W Y L Q K P G Q S P K L L I Y K V S
* * * * * * * *

CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTC AGTGGCAGTG GATCAGGGAC AGATTTTCACA
TTGGCTAAAA GACCCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
58 N R F S G V P D R F S G S G S G T D F T
* * * * *

301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT
78 L R I S R V E A E D L G L Y F C S Q S T
* * * * *

CDR #3

361 CATGTTCCGC TCACGTTCCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGTGCTGCA
GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCG ACAACGACGT
98 H V P L T F G A G T K L E L K R A V A A
* * * * *

421 CCAACTGTAT TCATCTTCCC ACCATCCAGT GAGCAATTGA AATCTGGAAC TGCCTCTGTT
GGTTGACATA AGTAGAAGGG TGGTAGGTCA CTCGTTAACT TTAGACCTTG ACGGAGACAA
118 P T V F I F P P S S E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCTCTCTCA CAGTGTCTCG TCCTGTCTGTT CCTGTCTGTT
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

FIG. 27A

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
 CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGCGAGT GTTCTCTCGAA GTTGTCCTCCCT
 198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTAA (SEQ ID NO.41)
 CTCACAATT
 218 E C O (SEQ ID NO.42)

FIG. 27B

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGATTTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
CGCATGCGAC TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
-3 A Y A E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTTCAGTA GCCACTACAT GCACTGGGTG
CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
18 V K I S C K A S G Y S F S S H Y M H W V
* * * *

CDR #1

181 AAGCAGAGCC ATGGAAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
TTCGTCTCGG TACCTTTCTC GGAATCACC TAACCGATGT AACTAGGAAG GTTACCACTT
38 K Q S H G K S L E W I G Y I D P S N G E
* * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
TGATGAATGT TGGTCTTTAA GTTCCCCTTC CGGTGTAAGT GACATCTGTG TAGAAGGTGC
58 T T Y N Q K F K G K A T L T V D T S S S
* * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
TCTCCCCTGA TATCTATGTT GCCGCTGACC AAAAAAGCTAC AGACCCCGCG TCCCTGGTGC
98 R G D Y R Y N G D W F F D V W G A G T T
* * * * *

CDR #3

421 GTCACCGTCT CCTCCGCCCTC CACCAAGGGC CCATCGGTCT TCCCCCTGGC ACCCTCCTCC
CAGTGGCAGA GGAGGCGGAG GTGGTTCCCG GGTAGCCAGA AGGGGGACCG TGGGAGGAGG
118 V T V S S A S T K G P S V F P L A P S S

481 AAGAGCACCT CTGGGGGCAC AGCGGCCCTG GGCTGCCTGG TCAAGGACTA CTTCCCCGAA
TTCTCGTGGA GACCCCCGTG TCGCCGGGAC CCGACGGACC AGTTCCTGAT GAAGGGGCTT
138 K S T S G G T A A L G C L V K D Y F P E

541 CCGGTGACGG TGTCGTGGAA CTCAGGCGCC CTGACCAGCG GCGTGCACAC CTTCCC GGCT
GGCCACTGCC ACAGCACCTT GAGTCCGCGG GACTGGTCGC CGCACGTGTG GAAGGGCCGA
158 P V T V S W N S G A L T S G V H T F P A

601 GTCCTACAGT CCTCAGGACT CTA CTCTCCCTC AGCAGCGTGG TGACCGTGCC CTCCAGCAGC
CAGGATGTCA GGAGTCCTGA GATGAGGGAG TCGTCGCACC ACTGGCACGG GAGGTCTGTCG
178 V L Q S S G L Y S L S S V V T V P S S S

FIG. 28A

661 TTGGGCACCC AGACCTACAT CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC
 AACCCGTGGG TCTGGATGTA GACGTTGCAC TTAGTGTTCG GGTGTTGTG GTTCCACCTG
 198 L G T Q T Y I C N V N H K P S N T K V D
 721 AAGAAAGTTG AGCCCAAATC TTGTGACAAA ACTCACACAT GA (SEQ ID NO.43)
 TTCTTTCAAC TCGGGTTTAG AACACTGTTT TGAGTGTGTA CT
 218 K K V E P K S C D K T H T O (SEQ ID NO.44)

FIG. 28B

Variable Light Chain Domain

	10	20	abcde	30	40	
6G425	DIVMTQTPLSLPVS LGDQASISCRSSQSLVHGIGNTYLHWYLQKPGQSPKLLIY					
	# # # # # # # # # #					
F(ab)-1	DIQMTQSPSSLSASV GDRVTITCRSSQSLVHGIGNTYLHWYQQKPGKAPKLLIY					
	# # # # # # # # # #					
humkI	DIQMTQSPSSLSASV GDRVTITCRASKTI-----SKYLAWYQQKPGKAPKLLIY					
	=====					
	+++++					
	L1					

	50	60	70	80	90	100	
6G425	YKVS NRFS GVPDR FSDSGSGTDFTLRISRVEAEDLGLYFCSQSTHVPLTFGAGTKLELKR						(SEQ ID NO.45)
	# # # # # # # # # #						
F(ab)-1	YKVS NRFS GVPDR FSDSGSGTDFTLTISLQPEDFATYYCSQSTHVPLTFGQGTKVEIKR						(SEQ ID NO.46)
	# # # # # # # # # #						
humkI	YSGSTLES GVPDR FSDSGSGTDFTLTISLQPEDFATYYCQQHNEYPLTFGQGTKVEIKR						(SEQ ID NO.47)
	=====						
	+++++						
	L2			L3			

Variable Heavy Chain Domain

	10	20	30	40	
6G425	EIQLQQSGPELMKPGASVKISCKASGYFSSHYMHVWKQSHGKSLEWI				
	# # # # # # # # # #				
F(ab)-1	EVQLVESGGGLVQPGGSLRLSCAASGYFSSHYMHVWRQAPGKLEWV				
	# # # # #				
humIII	EVQLVESGGGLVQPGGSLRLSCAASGFSFTGHWMNVWRQAPGKLEWV				
	=====				
	+++++				
	H1				

	50	a	70	80	abc	90	100	110		
6G425	GYIDPSNGETTYNQKFKGKATLTVDTSSTANVHLSSLTSDDSAVYFCAARGDYRYNGDWFFDVWGAGT									(SEQ ID NO.48)
	# # # # # # # # # #									
F(ab)-1	GYIDPSNGETTYNQKFKGRFTISRDN SKNTLYLQMN SLRAEDTAVYYCAARGDYRYNGDWFFDVWGQGT									(SEQ ID NO.49)
	# # # # # # # # # #									
humIII	GMIHPSDSETRYADSVKGRFTISRDN SKNTLYLQMN SLRAEDTAVYYCAARGIYFY-GTTYFDYWGQGT									(SEQ ID NO.50)
	=====									
	+++++					+++++				
	H2					H3				

FIG. 29

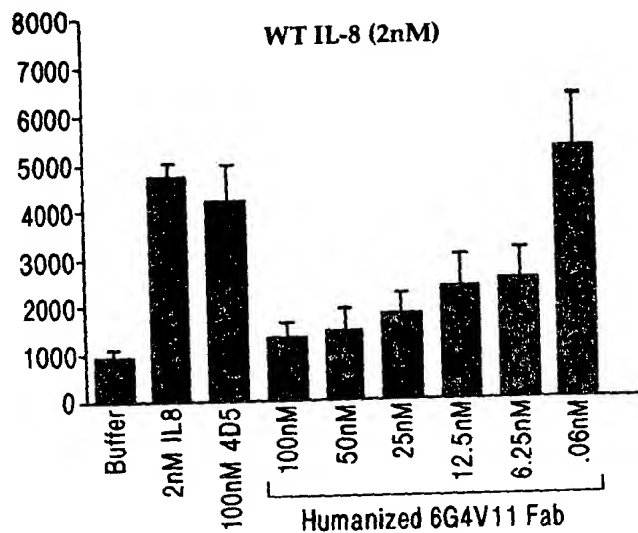


FIG. 30A

IC50~12nM

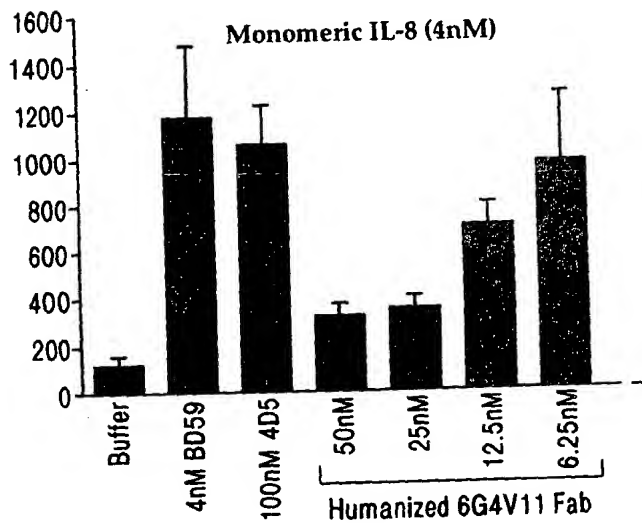


FIG. 30B

IC50~15nM

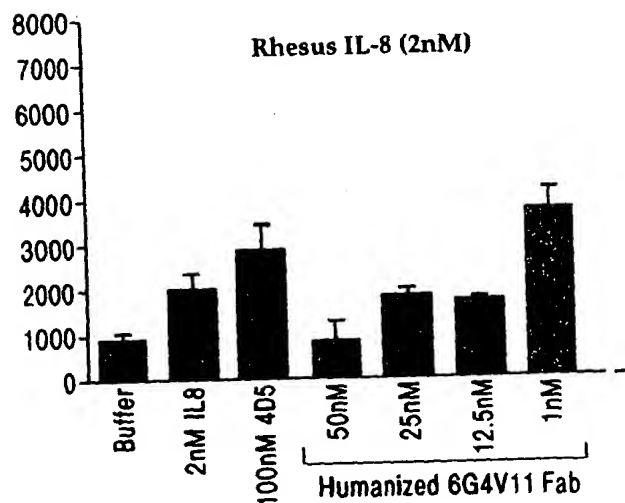


FIG. 30C

IC50~22nM

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Light Chain

MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTITCRSSQSLVHGIGNTY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGTDFTLTISLQPEDFATYYCSQST
HVPLTFGGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.51)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Heavy Chain

MKKNIAFLLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVRQAPGKGLWVGYYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFDFVWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHHKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.52)

Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

SGGGSGGDFDYEKMANANKGAMTENADENALQSDAKGKLDVATDYGAIDGFIGDVS
GLANGNGATGDFAGSSNSQMAQVGDGDN SPLMNNFRQYLPQLPQSVCECRPFVFSAGKPY
EFSIDCDKINLFRGVFAFLLYVATFMYVFTFANILRNKES (SEQ ID NO.53)

FIG. 31A

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTTCCTAT TGCTACAAAC
TACTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TAACACGTAT
TCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA
18 R V T I T C R S S Q S L V H G I G N T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATGAG GGTCTCTCA CAGTGTCTCG TCCTGTCTGT CCTGTCTGTG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGTAGT CCCGACTCG AGCGGGCAGT GTTTCCTGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TCGGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.51)

FIG. 31B

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTITCRSSQSLVHGIGNTY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGTDFTLTISSLPEDFATYCSQST
HVPLTEGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.51)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVKQAPGKGLEWVGVIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFFDVWGQGTLLTVTSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTISWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHHKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.55)

FIG. 31C



FIG. 32

TOP SECRET

FIG.
CLASS



Humanized Anti-IL3 Antibody

FIG. 32

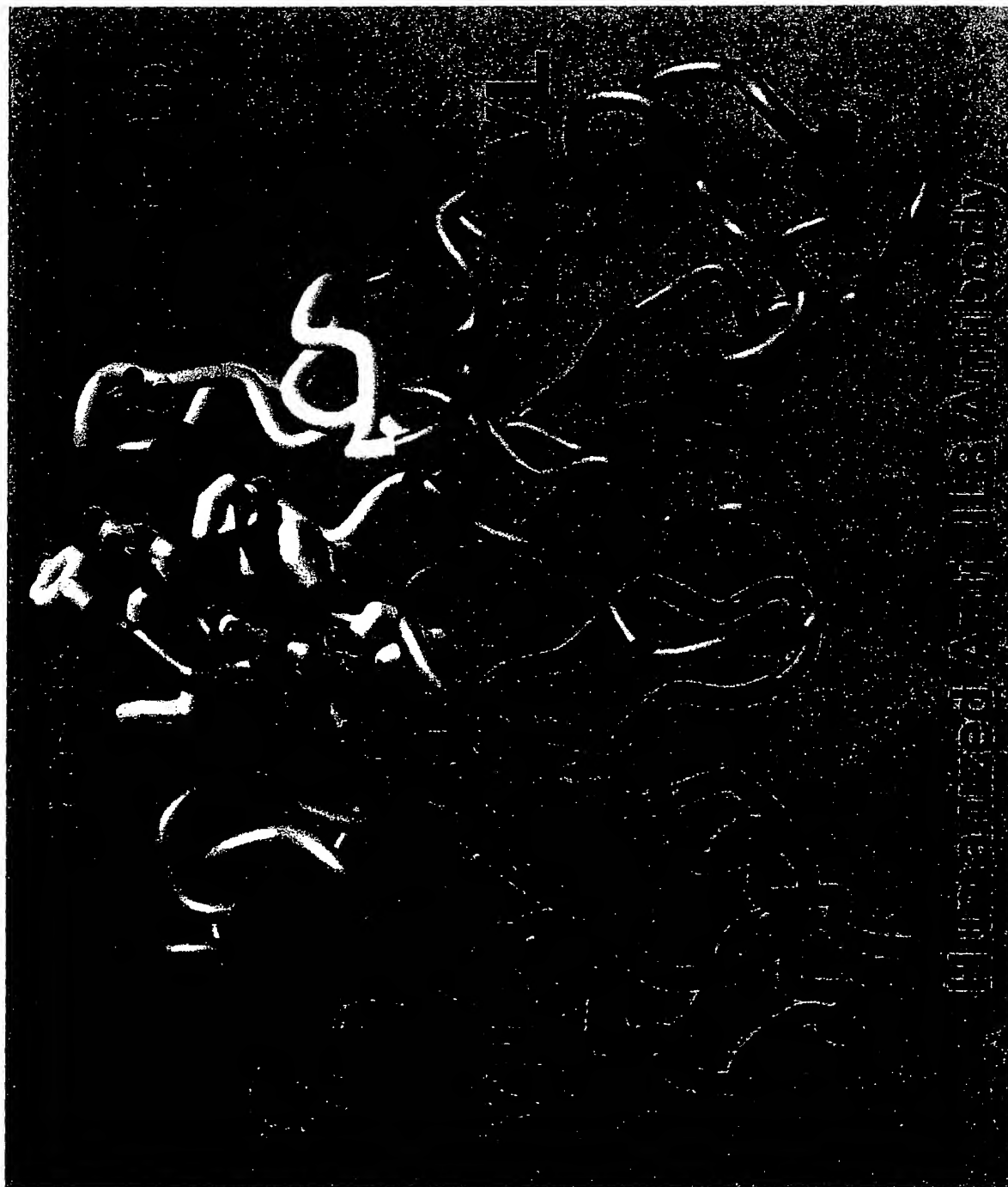


FIG. 32

FIG. 33

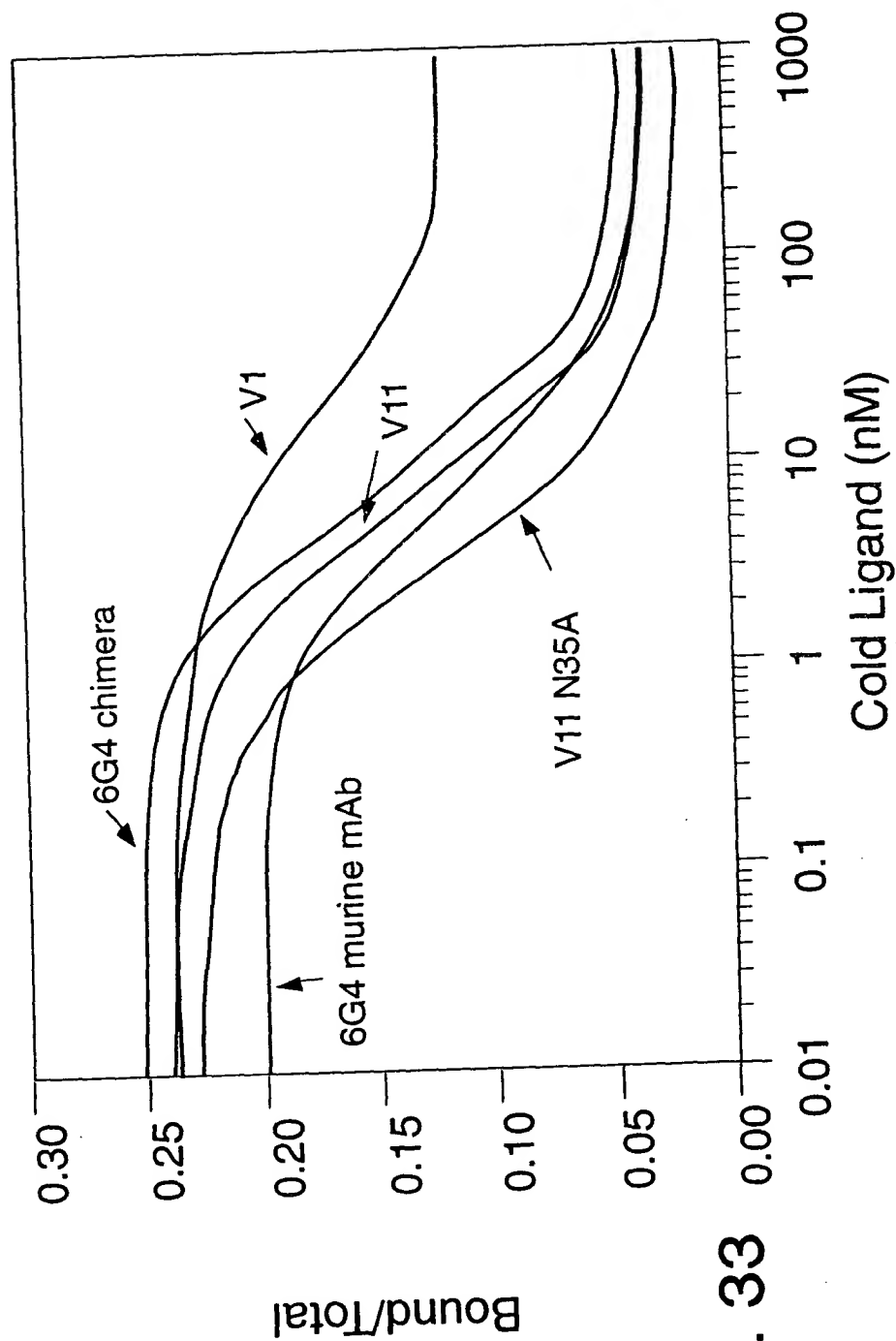
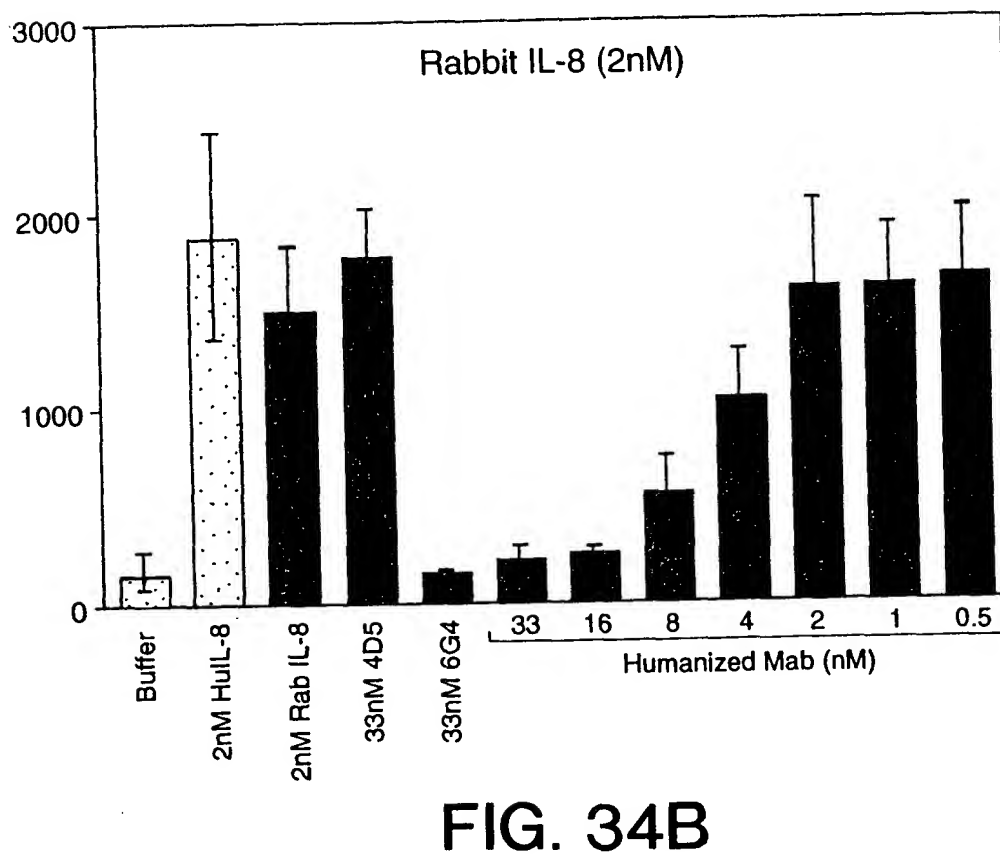
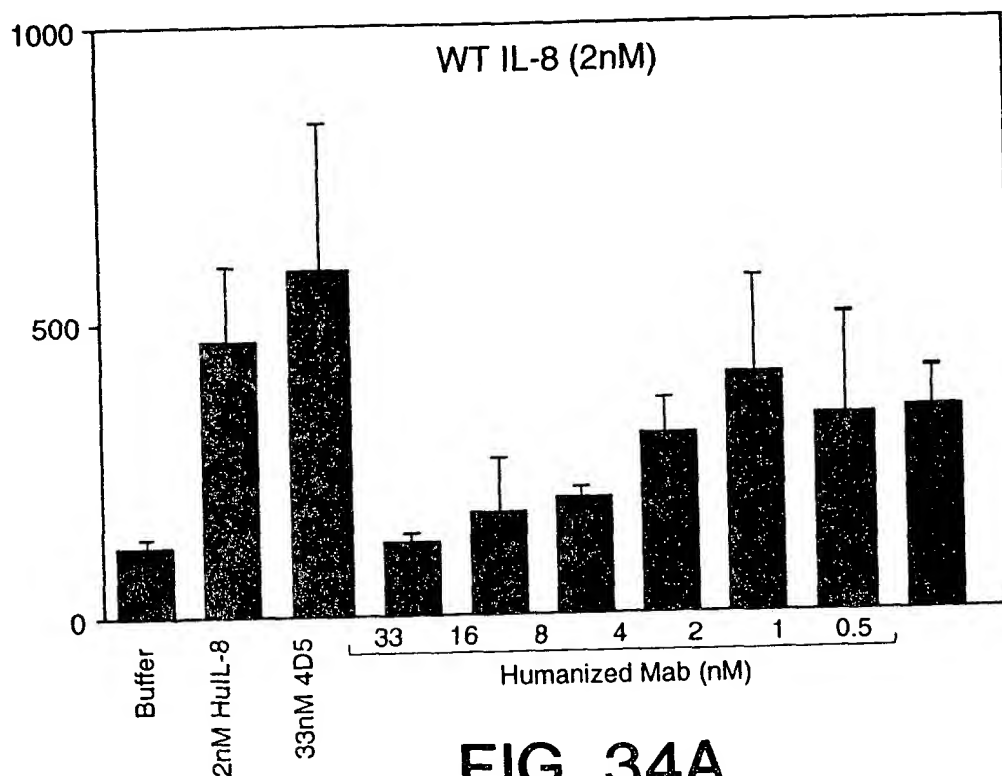
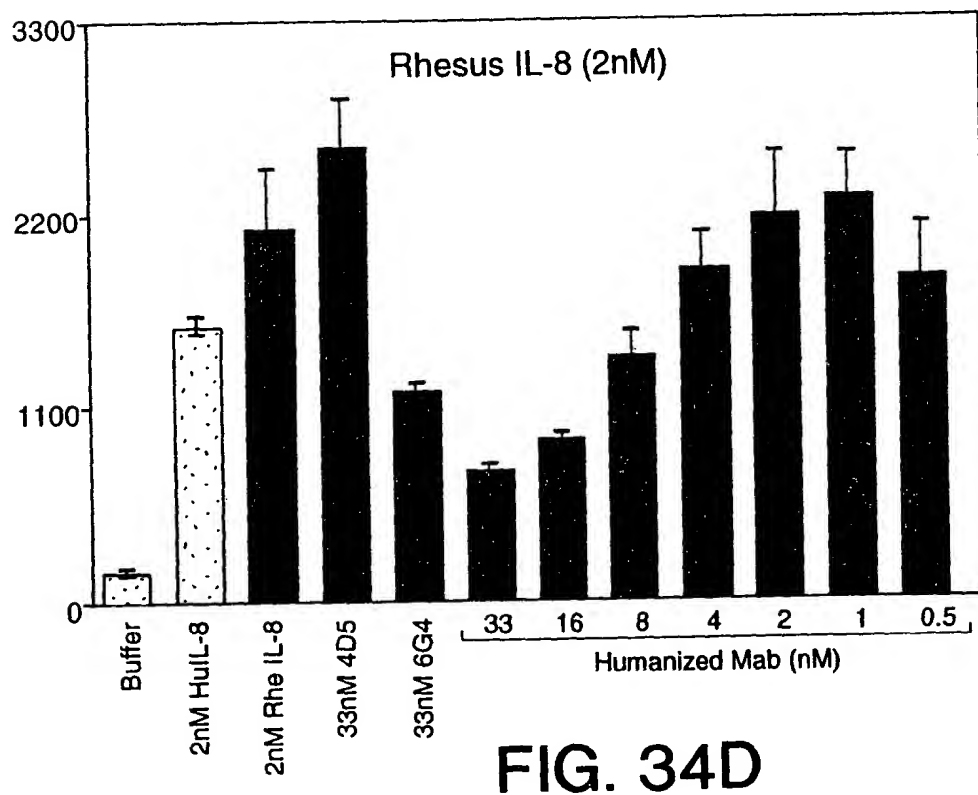
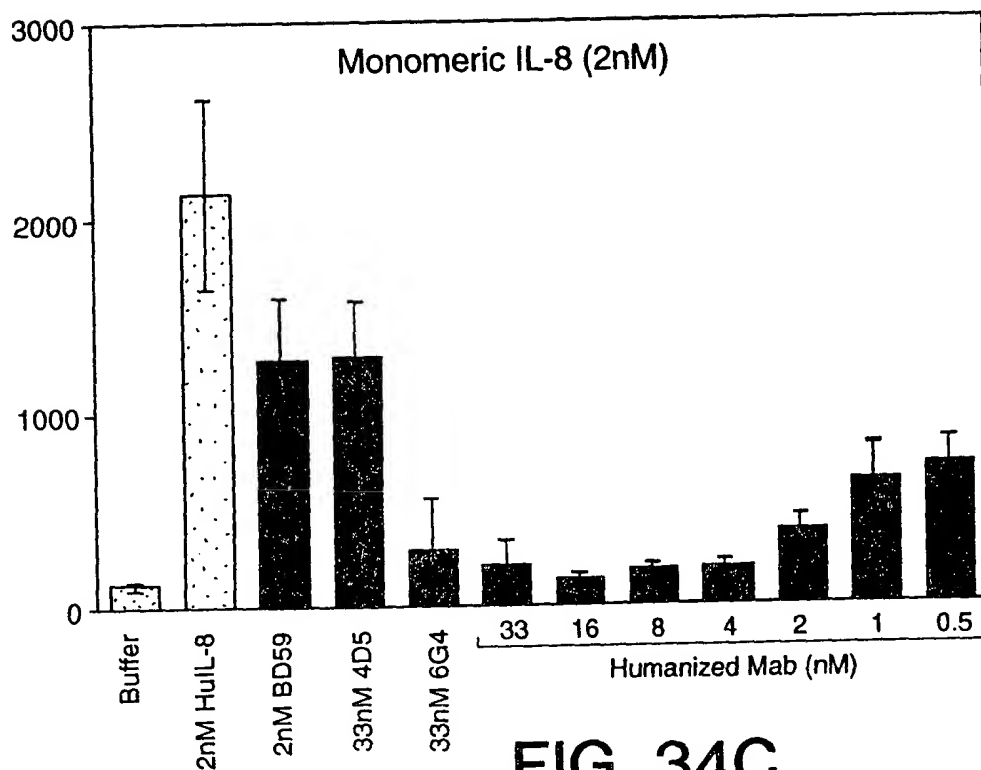


FIG. 33





TOP SECRET

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTITCRSSQSLVHGIGATY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGTDFTLTISSLQPEDEFAITYCSQST
HVPLTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.56)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVRQAPGKGLEWVGYYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFFDVWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.52)

Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPPCPAPELLGGRMKQLEDKVEELLSKNYHLENEVARLKKLVGER (SEQ ID NO.57)

FIG. 35

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGCTACGTAT
TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA
18 R V T I T C R S S O S L V H G I G A T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCTCTCTA CAGTGTCTCG TCCTGTCTGTT CCTGTCTGTTG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTCTCTGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G
(SEQ ID NO.58)

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TGCGGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.56)

FIG. 36

781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
TTTTCCCATA GATCTCCAAC TCCACTAAAA TACTTTTTTCT TATAGCGTAA AGAAGAACGT
-1 M K K N I A F L L A

841 TCTATGTTTCG TTTTCTCTAT TGCTACAAAC GCGTACGCTG AGGTTTCAGCT AGTGCAGTCT
AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
-11 S M F V F S I A T N A Y A E V Q L V Q S

901 GGCGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG
8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCACATATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCTGGAATGG
AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTCCC GGACCTTACC
28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTTCAA GTTCCCGGCA
48 V G Y I D P S N G E T T Y N O K F K G R

1081 TTCACTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
AAGTGAAATA GAGCGTGTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA
68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCCGTCTA TTACTGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG
CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCCCTAA TAGCGATGTT ACCACTGACC
88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
AAGAAGCTGC AGACCCAGT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG
108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGTG TCGCCGGGAC
128 P S V F P L A P S S K S T S G G T A A L

1321 GGCTGCCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
CCGACGGACC AGTTCTTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGCACAC CTTCCCCGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC
GACTGGTCGC CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCCTGA GATGAGGGAG
168 L T S G V H T F P A V L Q S S G L Y S L

1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
TCGTGCGACC ACTGGCACGG GAGGTCGTCG AACCCGTGGG TCTGGATGTA GACGTTGCAC
188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAGC CCAGCAACAC CAAGGTCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
TTAGTGTTTCG GGTGCTTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
208 N H K P S N T K V D K K V E P K S C D K

1561 ACTCACACAT GCCCCCGTG CCCAGCACCA GAACTGCTGG GCGGCCGCAT GAAACAGCTA
TGAGTGTTGA CGGGCGGCAC GGGTCGTGGT CTTGACGACC CGCCGGCGTA CTTTGTGCAT
228 T H T C P P C P A P E L L G G R M K Q L

FIG. 37A

FIG.
SUBCLASS

1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA
CTCCTGTTCC AGCTTCTCGA TGAGAGGTTC TTGATGGTGG ATCTCTTACT TCACCGTTCT
248 E D K V E E L L S K N Y H L E N E V A R

1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA (SEQ ID NO.59)
GAGTTTTTCG AACAGCCCCT CGCGATT
268 L K K L V G E R O (SEQ ID NO.60)

FIG. 37B

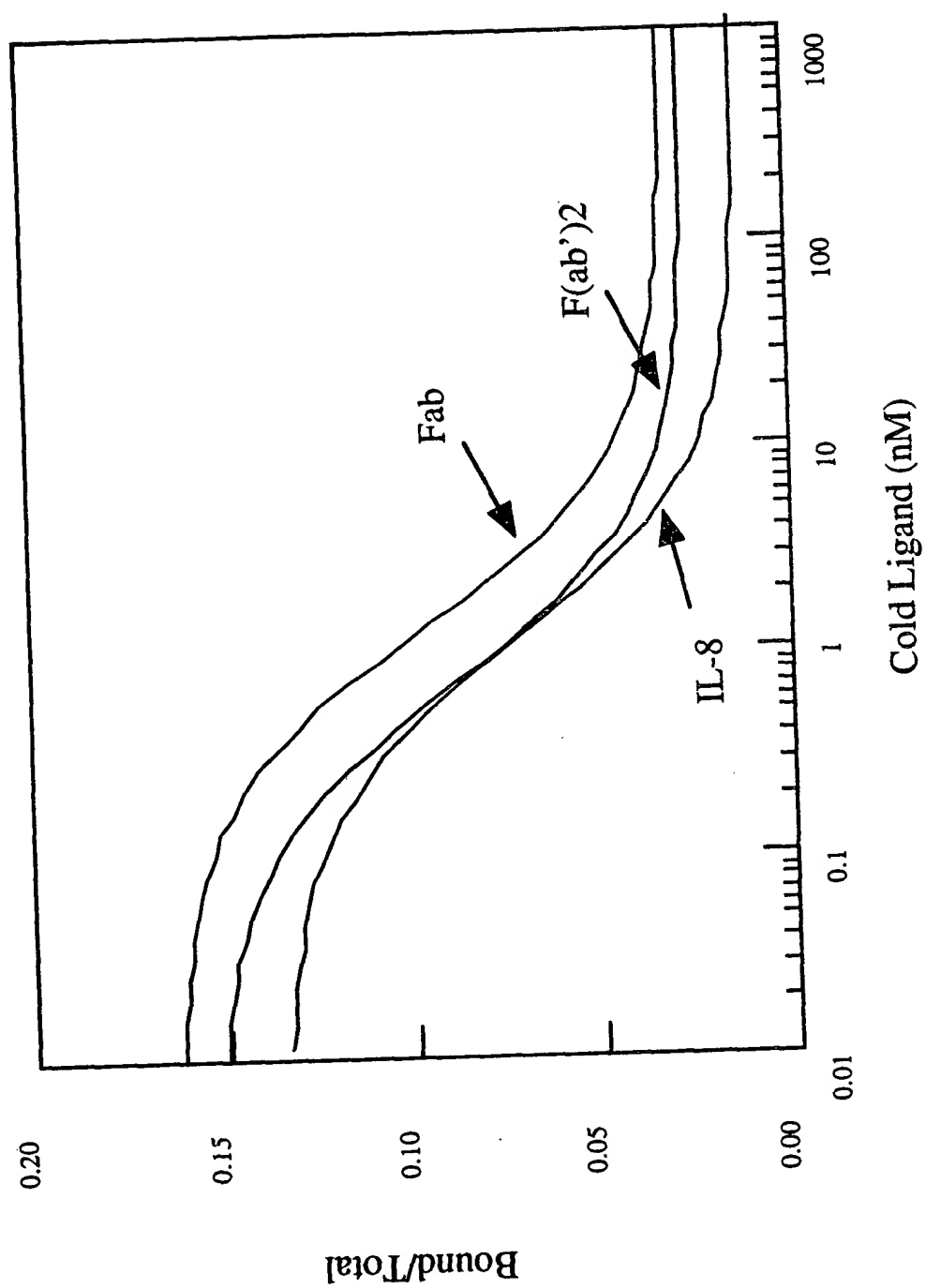


FIG. 38

FIG. 39

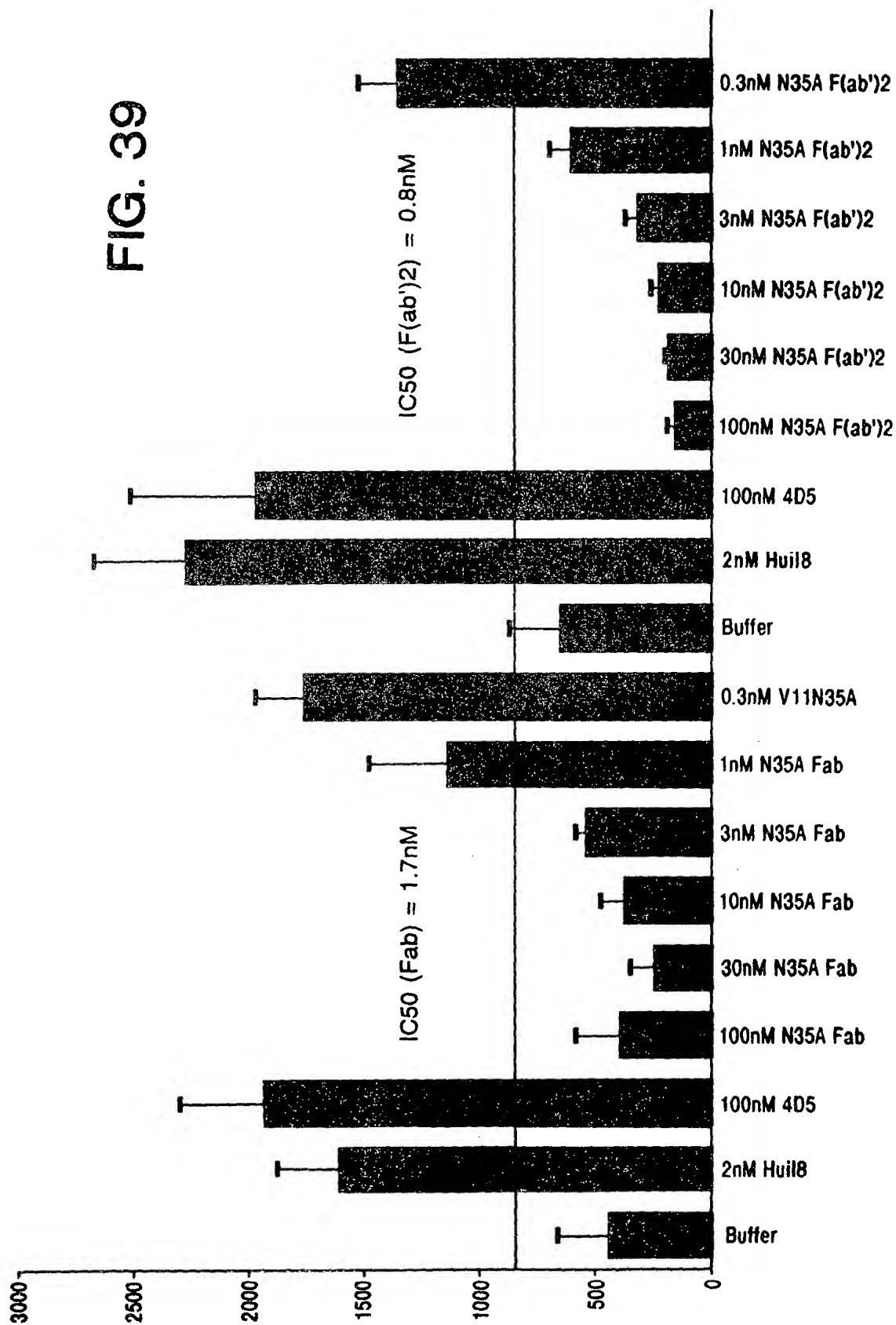


FIG. 40

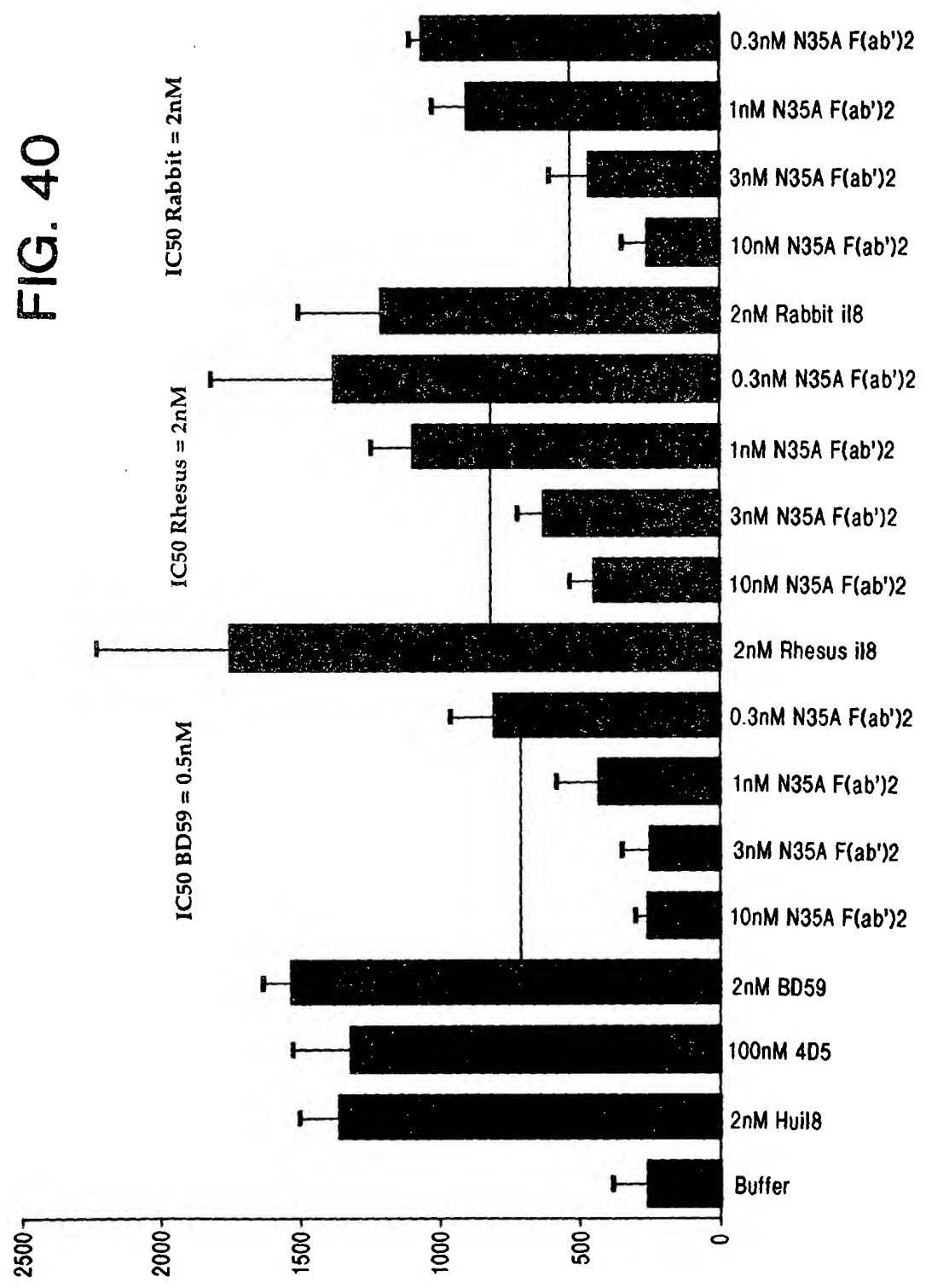


FIG. 41A

FIG. 41B

scrFI
ncII
mspI
hpaII
dsav
xmaI/pspAI
smaI
scrFI
ncII
dsav
cauII
bsaJI
avaI
sau3AI taqI
rsaI mboI/ndeII{dam-}
csp6I dpaI{dam+}
nlaIV nlaIV paer7I
kpnI cauII dpaII{dam-}
hgiCI bstYI/xhoII
bani bsaJI alwI{dam-}
asp718 bamHI avaI hphI
acc65I alwI{dam-} mnlI mnlI
401 TCGGTACCCG GGGATCCTCT CGAGGTTGAG GTGATTTTAT GAAAGAAT ATCGCATTC TTCTTGCATC TATGTTCTGTT TTTTCTATTG CTACAACGC
AGCCATGGGC CCTAGGAGA GCTCCAACCTC CACTAAATA CTTTCTTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC GATGTTGCG
M K K N I A F L L A S M F V F S I A T N A
a mutation was found that inactivated the mluI site. The penultimate nucleotide was changed fr G to T ^

sstI
sacI
hgiJII
hgiAI/aspHI
ecII136II
bspl286
bsiHKAI
bsmFI bmyI
bsrI avaI aluI
ecorV tthlII/aspi baniI
501 ATACGCTGAT ATCCAGATGA CCCAGTCCOC GAGCTCCTG TCCGCCTCTG TGGGCGATAG GGTCAACCATC ACCTGCAGGT CAAGTCAAG CTTAGTACAT
TATGCGACTA TAGGTCTACT GGGTCAGGGG CTCGAGGGAC AGGCGGAGAC ACCGCTATC CCAGTGGTAG TGGACGTCCA GTTCAGTTTC GAATCATGTA
-2 Y A D I Q M T Q S P S S L S A S V G D R V T I T C R S S Q S L V H

FIG. 41B

FIG. 41C

FIG. 41D

scfII
 nvaI
 ecorII
 dsav
 bstNI
 bsajI
 maeIII apyI[dcn+]

xmnI
 asp700
 caciI asp700
 TCTGGAAGTG CTTCTGTTGT GTGCTGCTG AATACTTCT ATCCAGAGAG GGCACAAAGTA CAGTGGGAGG TGGATAACGC CCTCCAATCG GGTAACTCCG
 AGACCTTGAC GAAGACAACA CACGGAGGAC TTATTGAAGA TAGGGTCTCT CCGGTTTCAT GTCACCTTCC ACCATTGCG GGAGGTTAGC CCATTGAGG
 132 S G T A S V V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q

haeIII/palI
 haeI
 mnlI
 csp6I
 mnlI
 bsaI
 mnlI
 bsaI
 maeIII apyI[dcn+]

fnu4HI
 bsoFI
 ddeI
 mnlI bbvI
 hgaI ddeI
 cellI/espI
 blpI/bpul102I
 accI caciI

maeIII
 1001 AGGAGAGTG CACAGAGCAG GACAGCAAGG ACAGCAGCTA CAGCCTCAGC AGCAGCCTGA CGCTGAGCAA AGCAGACTAC GAGAACACA AAGTCTACGC
 TCCTCTCACA GTGCTCTGTC CTGCTGCTCC TGCTGCTGAT GTGCTGCTG GTGCTGCTG GTGCTGCTG GTGCTGCTG GTGCTGCTG GTGCTGCTG GTGCTGCTG
 166 E S V T E Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A

cac8I
 aluI
 sstI
 sacI
 hgiJII
 hgiAI/aspHI
 ecl136II
 bsp1286
 bsiHRAI
 bmyI
 haeIII/palI
 sau96I banII
 asuI ddeI
 ecoO109I/draII
 hphI
 maeIII
 1101 CTGCGAAGTC ACCCATCAGG GCCTGAGTGC GCCGCTCACA AAGAGCTTCA ACAGGGGAGA GTGTTAAGCT GATCCTCTAC GCCGGAGCGA TCGTGGCCCT
 GACGCTCAG TGGGTAGTCC CGGACTCGAG CGGGAGTGT TTCTGCAAGT TGTCCTCTCT CACAATTCGA CTAGGAGATG CGGCTGCGGT AGCACCGGGA
 199 C E V T H Q G L S S P V T K S F N R G E C O (SEQ ID NO.56)

mnlI
 sau3AI
 mboI/ndeII[dam-]
 aluI dpaI[dam+] hgaI
 tru9I dpaI[dam-] mspI
 msel aluI[dam-] hpaII sfaNI
 sau96I
 haeIII/palI

rmaI
 maeI
 bfaI

FIG. 41D

FIG. 41E

1201 AGTACGCAAC TAGTCGTAAA AAGGTATCT AGAGTTGAG GTGATTTAT GAAAAGAAT ATCGCATTC TTCTGCATC TATGTTCTGTT TTTTCTATTG
 TCATGCCGTG ATCAGCATTT TTCCCATAGA TCTCCAACTC CACTAAATA CTTTCTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC
 M K K N I A F L L A S M F V F S I A

rsal
 bsiWI/splI
 thal
 fnuDII/mvni
 bstUI
 bsh1236I
 mluI csp6I mnlI
 aflIII ddeI
 rmai
 maeI
 bfaI
 aluI
 acil haeI
 bbiI
 banII
 bsp1286
 bstNI bsoFI
 apyI[dcn+] bsaJI bmyI
 haeIII/palI apyI[dcn+]
 dsav bstNI hgiJII
 bsoFI
 fnu4HI
 ecorII
 dsav
 scrFI
 mval
 ecorII
 dsav
 aluI
 alwNI[dcn-]
 fnu4HI
 bsoFI
 bbiI
 1301 CTACAAACGC GTACGCTGAG GTTCAGCTAG TGCAGTCTGG CGGTGGCTG GTGCAGCCAG GGGGCTCACT CCGTTTGTCC TGTGCAGCTT CTGGCTACTC
 GATGTTTGG CATGCGACTC CAAGTCGATC ACATCAGACC GCCACCGGAC CAGTCGGTC CCCCAGTGA GGCAACAGG ACACGTCGAA GACCGATGAG
 -5 T N A Y A E V Q L V Q S G G G L V Q P G G S L R L S C A A S G Y S

scrFI
 nciI
 mspI
 hpaII
 dsav
 cauII
 bslI
 xmaI/pspAI
 smaI
 scrFI
 nciI
 dsav
 cauII
 bslI

FIG. 41E

FIG. 41E

FIG. 41G

2101	GAGAAATCAAG	TGGCAAGACT	CAAAAAGCTT	GTCCGGGAGC	GCTAAGCATG	CGACGGCCCT	AGACTCCCTA	ACGCTCGGTT	CGCGCGGGC	GTTTTTTATT
	CTCTTACTTC	ACCGTCTCTGA	GTTTTTCGAA	CAGCCCTCG	CGATTCTAC	GCTGCCGGGA	TCTCAGGAT	TGCAGGCCAA	CGCGGGCCCC	CAAAAAATAA
262	E N E V	A R L	K K L	V G E R	O	(SEQ ID NO.60)				

[illegible]

FIG. 41H

FIG. 41I

2701 CTTGTTTCGG CGTGGGTATG GTGGCAGGCC CCGTGGCCGG GGGACTGTTG GGGCCATCT CCTTGCACGC ACCATTCTTT GCGCGCGCGG TGCTCAACGG
 GAACAAAGCC GCACCCATAC CACCGTCCGG GGCACCGGCC CCTTGACAAAC CCGCGGTAGA GGAACGTGCG TGCTAAGGAA CGCGCCGCCG ACAGTTGCC

[illegible]

FIG. 41J

FIG. 41K

FIG. 1

3201 CCCATTATGA TTCTTCTCGC TTCCGGCGGC ATCGGGATGC CCGCGTTGCA GGCCATGCTG TCCAGGCGAGG TAGATGACGA CCATCAGGGA CAGCTTCAAG bsmFI aluI alwI[dam-]
GGTAATACT AAGAAGACG AAGCGCGCG TAGCCTACG GCGCAACGT CCGGTACGAC AGTCCGTCCT ATCTACTGCT GGTAGTCCCT GTCGAAGTTC

3301 GATCGCTCGC GGCTCTTACC AGCCTAACTT CGATCACTGG ACCGCTGATC GTCACGGCGA TTTATGCCGC CTCGGCGAGC ACATGGAACG GGTGGCATG
CTAGCGAGCG CCGAGATGG TCGGATTGAA GCTAGTGACC TGGCGACTAG CAGTGCCGCT AAATACGGCG GAGCCGCTCG TGTACTTGC CCAACCGTAC

3401 GATTGTAGC GCGGCCCTAT ACCTGTCTGT CTTCCCGCGG TTGGCTCGG GTGCATGGAG CCGGGCCACC TCGACTGAA TGGAGCCCG CCGACCTCG
CTAACATCCG CCGCGGGATA TGGACAGAC GGAGGGGCGC AAGCAGCGC CACGTACCTC GGCCCGGTGG AGCTGGACTT ACCTCGGCC CCGTGGAGC

FIG. 41L

FIG. 41M

sau3AI
 mboI/ndeII{dam-}
 mamI{dam-}
 dpuI{dam+}
 dpuII{dam-}
 bstYI/xhoII
 alwI{dam-}
 mspI
 hpaII
 mroI bsaBI{dam-} fnu4HI
 bspMII bsoFI
 bspEI{dam-} bsvI
 bsaWI sfaNI
 accIII{dam-} foki cac8I
 mslI
 TTATGTTCCG GATCTGCATC GCAGGATGCT GCTGGGTACC
 AATACAAGGC CTAGACGTAG CGTCTTACGA CGACCGATGG
 3801 TGCTCTTCGG TTCCGTGTT TCGTAAAGTC TGGAACGCG GAAGTCAGCG CCCTGCACCA
 ACCAGAAGCC AAAGGCACAA AGCATTTTCAG ACCTTTGGC CTTCAGTCGC GGGACGTGGT
 acII
 thai
 fnuDII/mvni hinPI
 bstUI hhaI/cfoI
 bsh1236I haeII mslI
 cac8I
 hinPI
 hhaI/cfoI
 tru9I haeII
 mseI eco47III
 3901 CTGTGGAACA CCTACATCTG TATTAACGAA CGCTGGCAT TGACCCCTGAG TGATTTTCT CTGGTCCGC CGCATCCATA CGCCAGTTG TTTACCCCTCA
 GACACCTTGT GGATGTAGAC ATAATTGCTT CGGACCGTA ACTGGGACTC ACTAAAAGA GACCAGGGCG CGGTAGGTAT GCGGTCAAC AAATGGGAGT
 acII
 bsmFI foki
 sau96I sfaNI
 nlaIV acII
 avaiI fnu4HI bsri
 asuI bsoFI acII mnlI
 CTGGTCCGC CGCATCCATA CGCCAGTTG TTTACCCCTCA
 GCGGTCAAC AAATGGGAGT
 4001 CAACTTCCA GTAACCGGC ATGTTTCATCA TCAGTAACCC GTATCGTGAG CATCTCTCT CTGTTTCATCG GTATCATTAAC CCCATGAAC AGAAATTCOC
 GTTGAAGGT CATGGCCCG TACAAGTAGT AGTCATTGGG CATAGCACTC GTAGGAGAGA GCAAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGGG
 mnlI
 foki
 sfaNI
 maeIII
 psp1406I maeIII nspHI
 4001 CAACTTCCA GTAACCGGC ATGTTTCATCA TCAGTAACCC GTATCGTGAG CATCTCTCT CTGTTTCATCG GTATCATTAAC CCCATGAAC AGAAATTCOC
 GTTGAAGGT CATGGCCCG TACAAGTAGT AGTCATTGGG CATAGCACTC GTAGGAGAGA GCAAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGGG
 mnlI
 foki
 sfaNI
 maeIII
 psp1406I maeIII nspHI
 4001 CAACTTCCA GTAACCGGC ATGTTTCATCA TCAGTAACCC GTATCGTGAG CATCTCTCT CTGTTTCATCG GTATCATTAAC CCCATGAAC AGAAATTCOC
 GTTGAAGGT CATGGCCCG TACAAGTAGT AGTCATTGGG CATAGCACTC GTAGGAGAGA GCAAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGGG

FIG. 41N

FIG. 41Q

FIG. 41B

53701 GCAGAGTGG TCCTGCAACT TTATCCGCCT CCATCCAGTC ATTAATATGT TCGCGGGAAG CTAGAGTAAG TAGTTCCGCA GTTAATAGTT TCGCGCAACGT
CGTCTTCAAC AGGACGTTGA AATAGGCGGA GGTAGETCAG ATAAATTAACA ACGGCCCCCTC GATCTCATTC ATCAAGCGGT CAATTATCAA ACGCGTTGCA
sau96I mnII bsrI foki acII foki asei/asnI/vspI aluI bsrI mseI tru9I mstI psp1406I
avaII asuI

[illegible]

5901 ATGTTGTGCA AAAAAGCGGT TAGCTCCTTC GGTCTCCGA TCGTTGTGAC AAGTAACTTG GCCGAGTGT TATCACTCAT GGTATGGCA GCACATGCAT
TACAACACGT TTTTTCGCCA ATCGAGGAAG CCAGGAGGCT AGCAACAGTC TTCAATTCAAC CGGCTCACA ATAGTGAGTA CCAATACCGT CGTGACGCTAT
sau3AI
mboI/ndeII[dam-] acII
dpuI[dam+] fnu4HI
mnlI dpuII[dam-] bsoFI
sau96I pvuI/bspCI haeIII/palI fnu4HI
avaII mcrI eaeI nlaIII bsoFI
asuI bsiEI cfrI mslI bbvI

FIG. 41S

FIG. 41T

FIG. 41U

FIG. 41V

```
>length: 6563

aatII(GACGTC): 1645 6489
acc65I(GGTACC): 403 823
accI(GTMKAC): 1093 1963 4449
accII(TCCGGA): 3867[dam-]
acII(CCGC): 178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3367 3412
3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266
4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897
5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
acyI see hinII
afIIII(ACRYGT): 1307 4678
ageI(ACCGGT): 1788
ahaII/bsaHI(GRCGYC): 1645 1813 2616 2637 2751 3408 6107 6489
ahaII/draI(TTTAAA): 5435 5454 6146
ahdI/eam1105I(GACNNNNCTG): 346 5566
aluI(AGCT): 72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
2218 2233 2889 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
5922
alw44I/snoI(CTGCAC): 1831 4494 4992 6238
alwI[dam-](GGATC): 412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
6196 6214
alwNI[dcn-](CAGNNNNCTG): 1117 1385 5089
apaI(GGGCCC): 1695
apaLI/snoI(CTGCAC): 1831 4494 4992 6238
apoI(RAATTY): 1 391 4093
apyI[dcn+](CCWGG): 640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
aseI/asnI/vsPI(ATTAAAT): 5742
asnI see aseI
asp700(GAANNNTTC): 905 930 4234 6166
asp718(GGTACC): 403 823
aspHI see hgiAI
aspi see tthlII
asuI(GGNCC): 1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463
```

FIG. 41V

FIG. 42

Stop Template Primer

SL.97.2 5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3' (SEQ ID NO.63)

NNS Randomization Primer

SL.97.3 5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3' (SEQ ID NO.64)

FIG. 42

Randomization of Position N35 of Variable Light Chain CDR-1 Amino Acid Frequency

Phage Display (NNS Codon Library) Sort #3

Amino Acid	Frequency	% Total	IC50 (nM)
Asparagine (wt)	1	5.6	4.9
Glycine	6	16.6	3.1
Aspartic Acid	3	16.6	3.1
Glutamic Acid	4	22.2	0.1
Alanine	2	5.6	0.2
Lysine	1	5.6	ND
Serine	1	1.9	ND

FIG. 43A

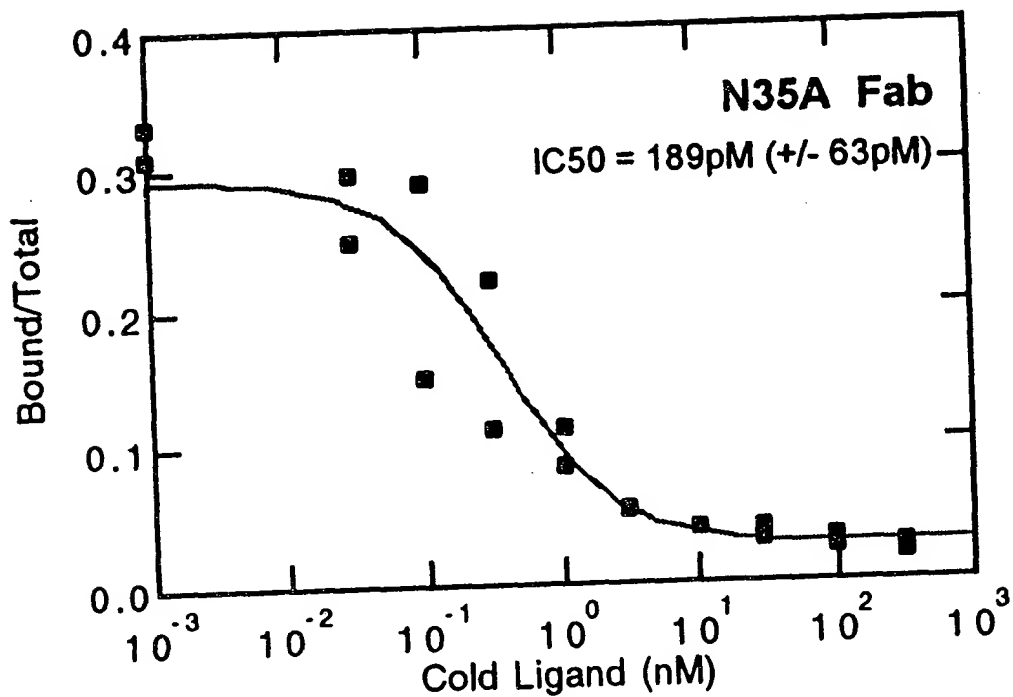


FIG. 43B

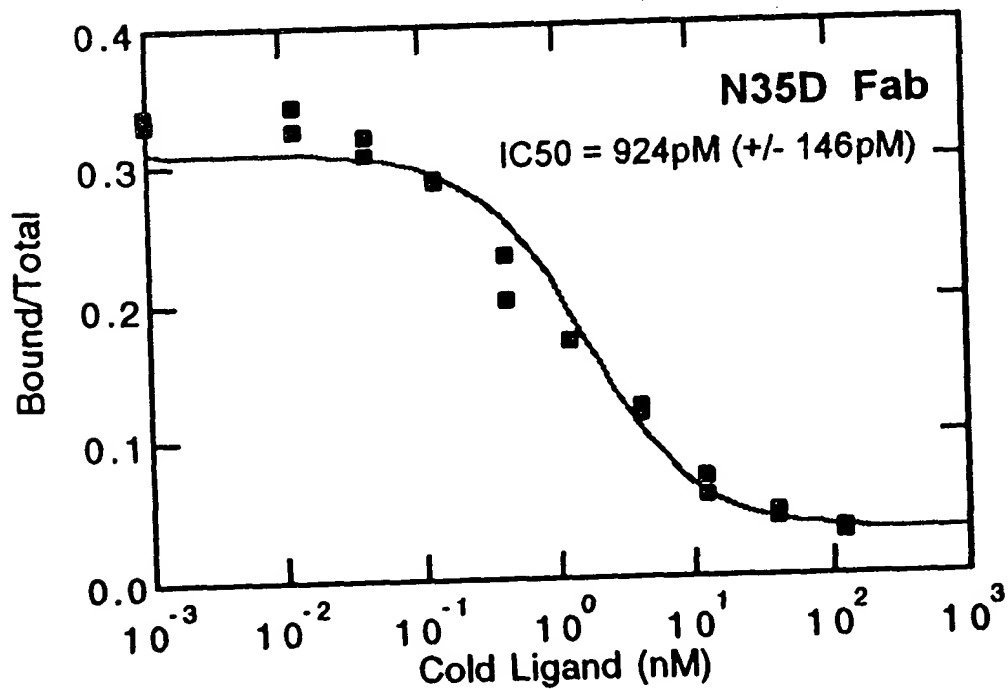


FIG. 43C

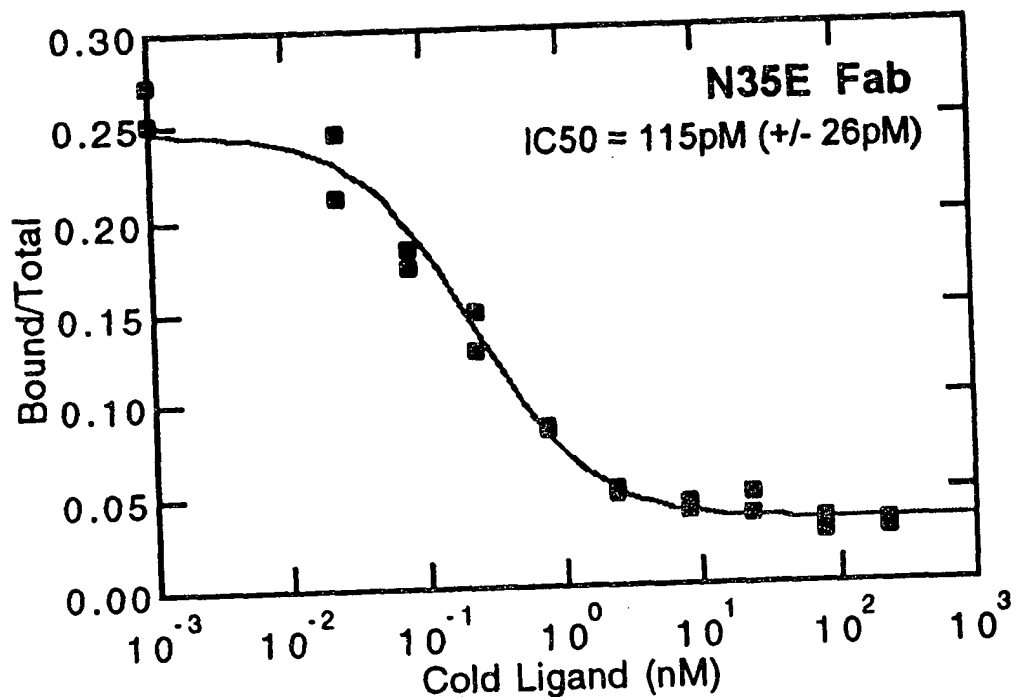


FIG. 43D

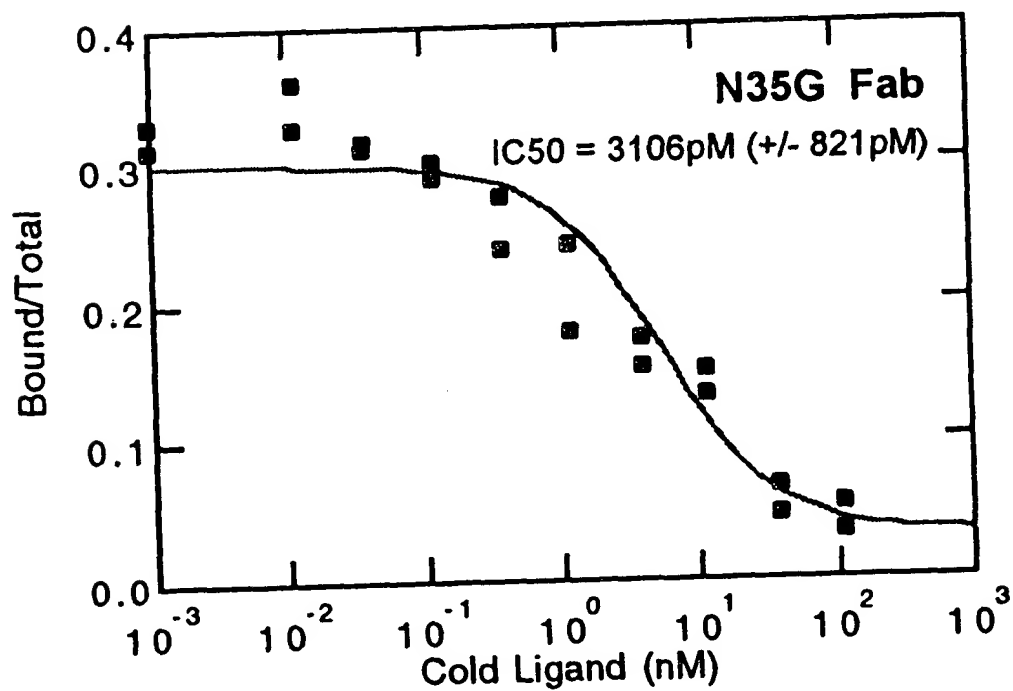
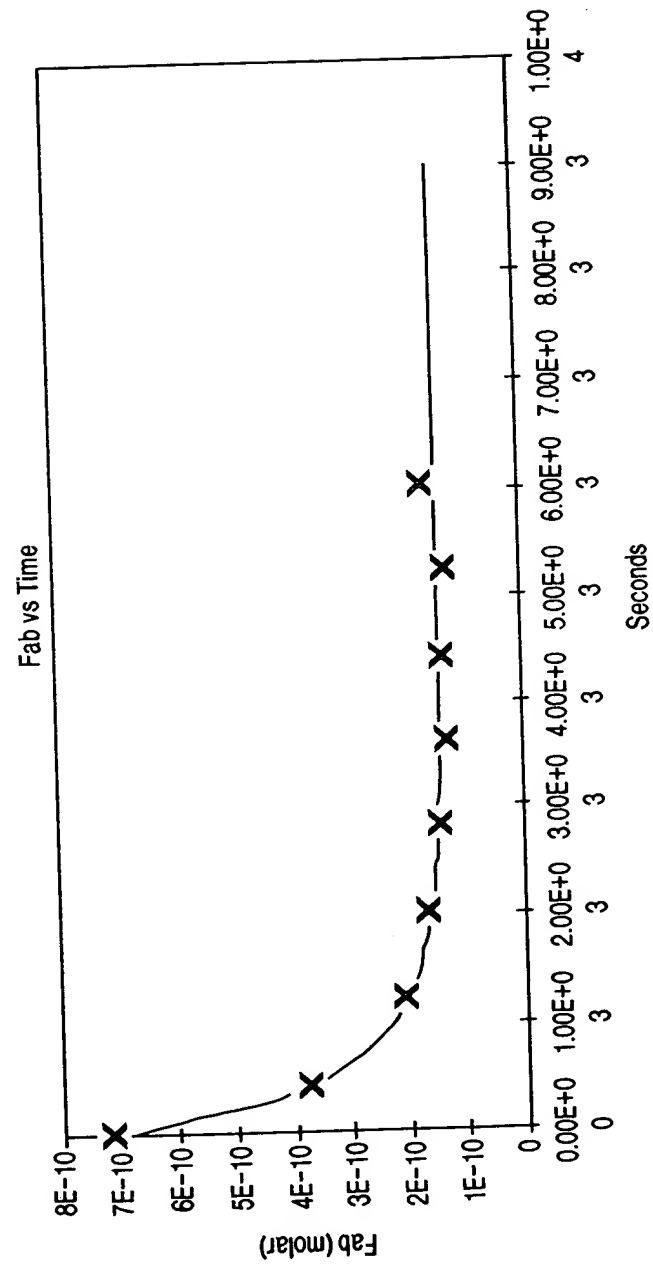


FIG. 43E

TOP SECRET



Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')₂

SAMPLE	ka	kd	Kd
6G4V11N35A-Fab	ND	ND	114pM
6G4V11N35A-F(ab') ₂	2.0x10 ⁶	2.1x10 ⁻⁴	109pM
6G4V11N35E-Fab	4.7x10 ⁶	2.6x10 ⁻⁴	54pM

FIG. 44

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGAGACGTAT
TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACTCTGCATA
18 R V T I T C R S S Q S L V H G I G E T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCCCTCTCA CAGTGTCTCG TCCTGTCTGTT CCTGTCTGTTG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTCTCTGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTG GACTAGGAGA TGCGGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.62)

FIG. 45

FIG. 46

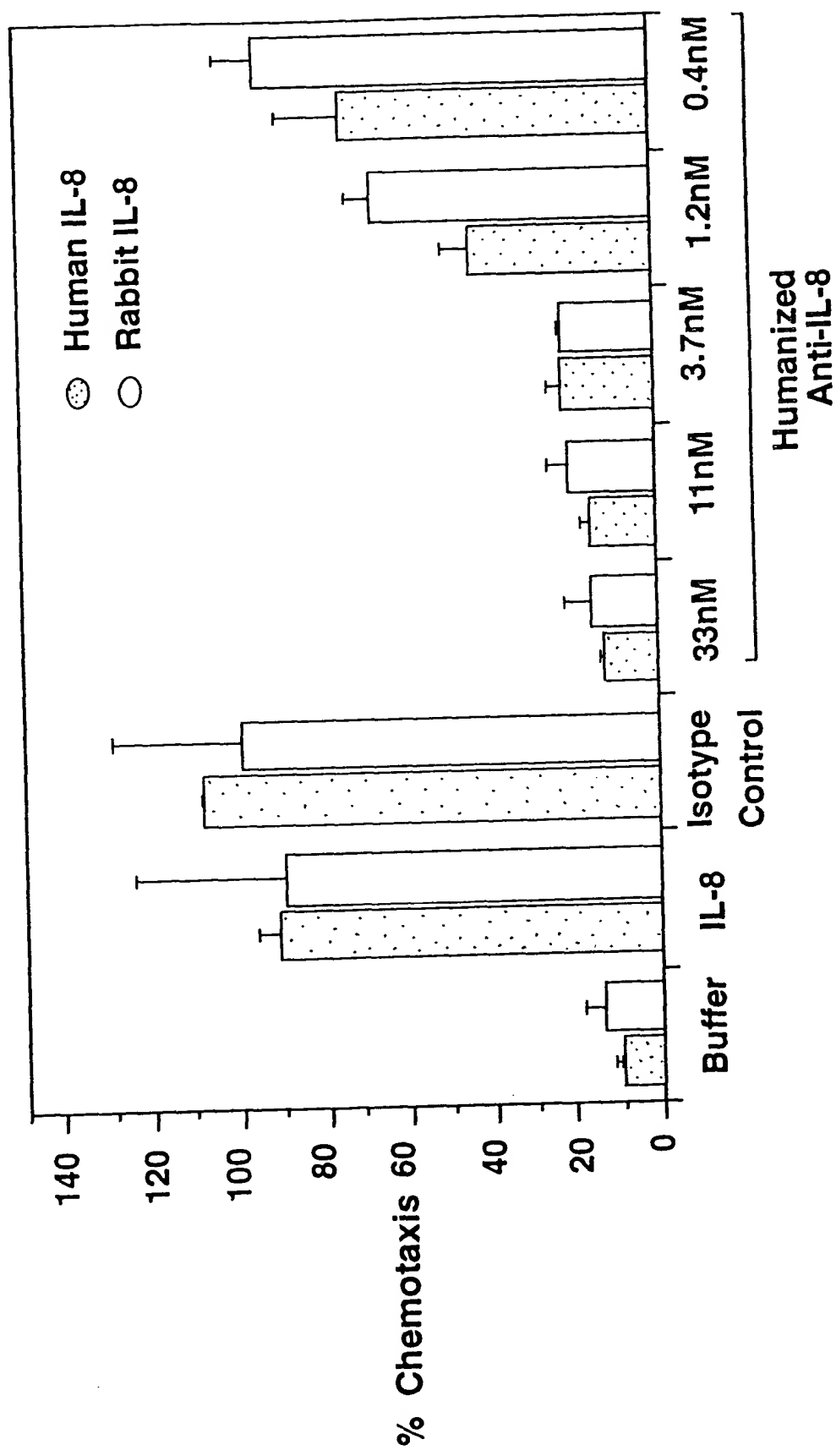


FIG. 46

FIG. 47

APPROVED	FIG.
DRAFT	SUCCESS

N35AH1upr

5'-CTAGTGCAGTCTGGCGGTGGTGCAGCCAGGGGGCTACTCCGTTTGTCTGTGCAGCTTCTGGCTACTCCTTC-3'
(SEQ ID NO.66)

N35AH1lwr

5'-TCGAGAAGGAGTAGCCAGAAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCAGGCCACCGCCAGACTGCAC-3'
(SEQ ID NO.67)

Bold indicates nucleotide change destroying PvuII site.

FIG. 47

```

cac8I
aluI
ssti
saci
hgiJII
hgial/aspHI
ecli36II
bsp1286
bsiHKAI
bmyI
baniI
taqi
sau3AI aluI
mboI/ndeII[dam-]
dpniI[dam+]
pvuI/bspCI
pleI dpniI[dam-]
hlnfi taqi[dam-]
rmaI mcrI pvuI
maei bseiI nspBII
bfaI taqi[dam-]
bsaFI nlaIV
bsmFI nlaIV
scrFI
mvaI
ecorII
dsav
bstNI
apyI[dcM+]
bsaJI
cac8I
TTCGAGTCG CCCGACATTG ATTATTGACT AGAGTCGATC GACAGCTGTG GAATGTGTGT CAGTTAGGTT GTGGAAGTCC CCAGCGGCTCC CCAGCAGGCA
AAGCTCGAGC GGGCTGTAAC TAATAACTGA TCTCAGCTAG CTGTGCACAC CTTACACACA GTCAATCCCA CACCTTTTCAG GGTCCGAGG GGTGCTCCGT

```

	sfaNI	scrFI	mvaI	scrFI	sfaNI					
	ppu10I				ppu10I					
	nsII/avaIII	mvaI		ecoRII	nsII/avaIII					
	nlaIII	ecoRII	dsav		nlaIII					
	sphI	dsav	bstNI		sphI					
	nsPI	bstNI		apyI[dcM+]	nsPI					
	nsPHI	apyI[dcM+]	bsaJI		nsPHI					
	cac8I	sexAI	bsmFI	nlaIV	cac8I					
101	GAGCATGCA	AAGCATGCAT	CTCAATTACT	CAGCAACCAC	GTGTGGAAAG	TCCCCAGGCT	CCCCAGCAGG	CAGAAGCTATG	CAAGACATGC	ATCTCAATTAT
	CTTCATACGT	TTCGTAGCTA	GAGTTAATCA	GTCCGTGGTC	CACACCTTTC	AGGGTGCGGA	GGGTGCGTCC	GTCTTCTATAC	GTITTCGTAGC	TAGAGTTAAT

201 GTCAGCAACC ATAGTCCCGC CCGTAACTCC GCCCATCCCG CCCCTAACTC CGCCAGTTC CGCCATTCT CGCCCCATG SCTGACTAAT TTTTTTTATT
 CAGTCGTGG TATCAGGCG GGGATTGAG CGGGTAGGG GGGGATTGAG GGGGTCAG GCGGTGAGA GCGGGGTAC CGACTGATTA AAAAAAATAA

FIG. 48A

FIG. 48B

FIG. 48C

```

601 CAAAGAAATGA CCACAACCTC TTCAGTGGAA GGTAAACAGA ATCTGGTGAT TATGGGTAGG AAAACCTGGT TCCTCCATTCC TGAGAGAAT CGACCTTTAA
    GTTTCTTACT GGTGTTGGAG AAGTCACCTT CCATTGTCT TAGACCACCTA ATACCATCC TTTTGGACCA ACAGGTAAGG ACTCTTCTTA GCTGGAAT
    eco57I      mboII      earI/ksp632I      mnII      tfII      hinfI      hphI      alwNI[dcM-]      apyI[dcM+]      bstNI      sexAI      ddeI      mboII      taqI      ahaII/draI      trn9I      mseI
    scrFI      mvaI      ecorII      dsav      bstNI      apyI[dcM+]      sexAI      ddeI      mboII      taqI      ahaII/draI      trn9I      mseI
    sstI      sacI      hglJII      hglAI/aspHI      eclI36II      bspI286      bsiHKA1      bmyI      mnII      aluI      bssSI      banII      bstXI      foki      sfanI      mseI      afaII/bfRI      trn9I
    701 AGGACAGAAT TAATATAGT CTCAGTAGAG AACTCAAGAG ACCACCACGA GGAGCTCATT TTCTTGCCAA AAGTTGGAT GATGCCCTAA GACTTATTGA
    TCCCTGTCTTA ATTATATCAA GAGTCATCTC TTGAGTTTCT TGGTGGTGCT CCTCGAGTAA AAGAAGGCTT TTCRAACCTA CTACGGAAT CTGAATAACT
    trn9I      mseI      ddeI      aseI/asnI/vspI      bsaI      bseRI      mnII      aluI      bssSI      banII      bstXI      foki      sfanI      mseI      afaII/bfRI      trn9I
    801 ACAACCGGAA TTGGCAAGTA AAGTAGACAT GGTGTTGGATA GTTCTGTTTA CCAGGAGCC ATGAATCAAC CAGGCCACCT TAGACTCTTT
    TGTTGGCCTT AACCGTTTAT TTATCTCTGA CCAACCTAT CAGCTCCGT CAAGACAAAT GGTCTTCGG TACTAGTTG GTCCGGTGGA ATCTGAGAAA
    mspI      hpaII      bsaWI      accI      nlaIII      mnII      scrFI      mvaI      ecorII      dsav      bstNI      nlaIII      betNI      ddeI      pleI      hinfI
    haeIII/paII      haeI

```

FIG. 48C

FIG. 48D

hgal
 hinli/acyl
 ahail/bsaHI
 scrFI
 mval
 ecoRII
 dsav
 bstNI
 apyI[dcmt+] mnlI
 bsajI bsli ddel
 mnlI
 901 GTGACAAGGA TCATCCAGGA ATTTGAAGT GACACGTTTT TCCACAGAAAT TCATTTGGGG AAATATAAAC CTCTCCAGGA ATACCCAGGC GTCTCTCTG
 CACTGTTCT AGTAGTCCT TAACTTTCA CTGTGCAAAA AGGTCTTTA ACTAAACCC TTTATATTG GAGAGGGTCT TATGGGTCCG CAGGAGAGAC

scrFI
 mval
 ecoRII
 dsav
 bstNI
 apyI[dcmt+]

sau96I
 avall

1001 AGTCCAGGA GGAAGAAGGC ATCAAGTATA AGTTGAAGT CTACGAGAAG AAGACTAAC AGAAGATGC TTTCAGATTC TCTGTCCTCC TCTTAAGCT
 TCCAGGTCCT CCTTTTCCG TAGTTCATAT TCAAACTTCA GATGCTCTC GATGCTCTC TTTCTGATTG TCCTTCTACG AAGTTCAAG AGACGAGGGG AGGATTTCGA
 ^END DHR

styI
 bsajI
 sau3AI
 mboI/ndelI[dam-]
 dplI[dam+]
 dplI[dam-]
 alwI[dam-]
 bstYI/xhoII
 cac8I
 ppulOI
 nsiI/avallI
 1101 ATGCAATTTT ATAACACCAT GGGACTTTTG CTGGCTTTAG ATCCCTTTGG CTTCGTTAGA ACCGAGGTAC AATTAATACA TAACCTTATG TATCATACAC
 TACGTAAAAA TATTCTGGTA CCTGTAAAAA GACCGAAATC TAGGGGAACC GAACCAATCT TCGTCGATG TTAATTATGT ATTGGAATAC ATAGTATGTG

sau96I
 avall
 asul
 scrFI
 mval
 ecoRII

FIG. 48D

nlaIII
 styI
 pflMI
 ncoI
 dsal
 bslI foki
 bsaI
 nlaIII foki
 TTCTAGTACG AACTGCAACT GGAGTACATT CAGAACTTCA GATAGTGCAG TCTGGCGGTG GCGTGGTCCA
 1301 CCACCATGGG ATGGTCAATG ATCATCCCTTT
 GGTGGTACCC TACCAGTACA TAGTAGGAAA AAGATCATCG TTGACGTTGA CCTCATGTAA GTCCTCAAGT CGATCACGTC AGACCGGCAC CGGACCAAGT
 E V Q L V Q S G G G L V Q
 1

FIG. 48E

FIG. 48F

FIG. 48G

1801 CTGGGCTGCC TGGTCAAGGA CTACTTCCCG GACCGGTGA CGGTGCTGTG GAATCAGGC GCGGTGACCA CCGGTGACCA CACCTTCCCG GCTGCTCTAC
GACCCGACGG ACCACTTCCCT GATGAAGGG CTTGGCCACT GCCACAGCAC CTTGAGTCGG CGGACTGGT CGCGGACGCT GTGGAAGGCG CGACAGGATG
147 L G C L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q

scrFI mvaI hgiAI/aspHI hinPI nlaIV nari kasi hpiI/acyI bmyI mspI hpaII
ecorII bsp1286 bsiHKAII bmyI cac8I scrFI fnu4HI nciI
dsav betNI bsaII haeII bani ahaII/bsaHI acII apaII/snoI dsav mspI
bsaI cfr10I/bsrFI bsaWI egeI tth111I/aspI ddei hhai/cfoI nspBII alw44I/snoI cauli scfI
apyl{dcm+} bsoFI bsaWI bsaII/bsaHI acII apaII/snoI dsav mspI hpaII
fnu4HI bsoFI bsaWI egeI tth111I/aspI ddei hhai/cfoI nspBII alw44I/snoI cauli scfI
bbvI

1901 AGTCTCAGG ACTTACTCC CTCAGCAGCG TGGTACTGT GCCCTTAGC AGCTTGGCA CCCAGACCTA CATCTCAAC GTGAATCACA AGCCAGCAA
TCAGGAGTCC TGAGATGAGG GAGTCGTCGC ACCACTGACA CGGAGATCG TCGAACCGT GGTCTGGAT GTAGAGCTTG CACTTAGTGT TCGGTCGTT
181 S S G L Y S L S S V T V P S S S L G T Q T Y I C N V N H K P S N

fnu4HI bsoFI nlaIV hgiCI tfil
bsoFI rmai bsp1286 maeI bani hinfi
maeIII hpiI bmyI mnlI bmyI maeI
hpiI bmyI mnlI bmyI maeI

ahdI/eam1105I
sau96I
avaII

2001 CACCAAGGTG GACACAAAG TTGAGCCCAA ATCTTGTGAC AAAACTCACA CATGCCACCG GTGCCAGCA CCTGAACCTC TGGGGGACC GTCAGTCTTC
GTGGTCCAC CTGTTCTTTC AACTCGGGT TAGAACACTG TTTTGTGTGT GTACGGGTGG CACGGGTGGT GGACTTGAGG ACCCCCTGG CAGTCAGAAG
214 T X V D K K V E P K S C D K T H T C P A P E L L G G P S V F

hgiJII bsp1286 mspI nspI bsaJI bsmFI mboII
bsaJI bmyI bani bmyI alwNI{dcm-} apyl{dcm+} bbsI mnlI
mslI

scrFI mvaI asuI ecorII dsav bstNI nlaIV mboII
bsaJI bsmFI bbsI mnlI

FIG. 48G

acII
thai
fnuDII/mvni
bstUI
bsh1236I
sacII/sstII
nspBII
kspI
dsaI
bsaJI
maeII
rsaI
csp6I
bsrI bsaAI
fnu4HI
bsaJI
bseKI
mnII

[illegible]

FIG. 48H

FIG. 48I

```

scrFI      nciI      mspI      hpaII      dsav      cauli
xmaI/pspAI
smaI      scrFI      nciI      dsav      cauli
rsal      foki
bslI      bsaJI      mboII
bsp1407I/bsrGI      bslI      auaI      earI/kep632I
2401 CAGCCCCGAG AACACAGGT GTACACCCCTG CCCCCATCCC GGAAGAAGAT GACCAAGATC CAGGTGAGCC TGACCTGCTT GGTCAAAGGC TTCTATCCCA
GTCCGGGGCTC TTGGTGTCCA CATGTGGGAC GGGGGTAGGG CCCTTCTCTA CTGGTCTTGT CTCCAGTCGG ACTGGACGGA CCAGTTTCCG AAGATAGGCT
347 Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S

mspI      hpaII
fnu4HI      bsoFI      bsvI
bsrDI      bsaJI
2501 CGCACATGCG CGTGGAGTGG GAGAGCAATG GGCAGCCGGA GAACAACATC AAGACCAGC CTCCCGTGGT GACTCCGAC GGCTCCTTCT TCCTCTACAG
CGCTGTAGCG GCACCTCACC CTCTCGTTAC CCGTCGGCCT CTGTGTTGATG TTCTGGTGG GAGGGACGA CCTGAGGCTG CCGAGGAAGA AGGAGATGTC
381 D I A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S

mboII      bpuAI      maelI      xmnI      bbsI      nlaIII      sfaNI      mnlI
asp700      nlaIII      sfaNI      mnlI
2601 CAAGCTCACC GTGACAAGA GCAGTGGCA GCAGTGGCA GTCTTCTCAT GTCCCGTGTGAT GCATGAGGCT CTGCACAACC ACTACACGCA GAAGAGCCTC
GTTCGAGTGG CACCTGTTCT CGTCACCGT CGTCCCGCTT GAGAAGACTA CGAGGCACCTA CGAGGCACCTA CGAGGCACCTA CGAGGCACCTA CGAGGCACCTA
414 K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L

sapi      mboII      mnlI
earI/kep632I
GAAGAGCCTC
CTTCTCGGAG

```

FIG. 48I

FIG. 48J

FIG. 48K

TTTGGCTTT

3301 AGGAGGCTTT TTTGGAGGCC TAGGCTTTTG CAAAAGCTA GCTTATCCGG CGGGGAACGG TGCATTGGAA CGCGGATTCC CGGTGCCAAG AGTCAGGTAA
TCCTCCGAAA AARACCTCCGG ATCCGAAAC GTTTTTCGAT CGAATAGGCC GGCCTTGGCC ACGTAACCTT GCGCTTAAGG GGCACGGTTC TCAGTCCATT
^seq from pSV16B5-6G4VL: AvrII - HindIII frag
^U1 matched splice donor^

rmal mael styI bsaJI blnI avrII(dam-) haeIII/pali stuI haeI mnlI bfaI mnlI mnlI bfaI
scfI mcrI aluI rmaI mael bfaI nheI cac8I aluI mnlI bfaI
nclI eagi/xmaII/eclXI eaeI cfrI bsiEI mspI caulI hpaII
mspi hpaII dsav haeIII/pali mcrI aluI rmaI mael bfaI nheI cac8I aluI mnlI bfaI
tfII hinfi acII thal fnuDII/mvni bstUI bsh1236I pleI hinfi

3401 GTACGGCCTA TAGAGTCTAT AGGCCACCC CCTTGGCTTC GTTAGAACGG GGCTACAAAT AATACATAAC CTTTGGATC GATCCTACTG ACACGTGACAT
CATGGCGGAT ATCTCAGATA TCCGGGTGGG GGAACCGAAG CAATCTGGC CGATGTAA TTATGTATTG GAAACCTAG CTAGGATGAC TGTGACTGTA
^sp6 promoter
^U2 match
lariat consensus^
IgG VH natural lariat restored^

acII rsal csp6I scfI pleI haeIII/pali bsaJI bfaI mnlI bfaI mnlI mnlI bfaI
scfI mcrI aluI rmaI mael bfaI nheI cac8I aluI mnlI bfaI
nclI eagi/xmaII/eclXI eaeI cfrI bsiEI mspI caulI hpaII
mspi hpaII dsav haeIII/pali mcrI aluI rmaI mael bfaI nheI cac8I aluI mnlI bfaI
tfII hinfi acII thal fnuDII/mvni bstUI bsh1236I pleI hinfi
sau3AI mboI/ndeII(dam-) dpnI(dam+) dpnII(dam-) alwI(dam-) taqI(dam-) clai/bspl06(dam-) bspDI(dam-) sau3AI
mboI/ndeII(dam-) dpnI(dam+) dpnII(dam-) alwI(dam-) foki
CTTTTGGATC GATCCTACTG ACACGTGACAT
GAAACCTAG CTAGGATGAC TGTGACTGTA
^removed ATG

FIG. 48L

[illegible][illegible][illegible][illegible]

FIG. 48M

FIG. 48N

TTTGGG" GGGGGGGG

```

rsal      mnlI      maeIII bsaJI      maeIII      scrFI      fnu4HI
csp6I     bslI      maeIII bsaJI      maeIII      mval      ddel bsoFI
4101 AGTACAGTGG AAGGTGGATA ACGCCCTCCA ATCGGGTAAC TCCAGGAGA GTCTCACAGA GCAGGACAGC AAGGACAGA CCTACAGCCT CAGCAGCACCC
TCATGTCACC TTCACCTAT TCGCCGAGGT TAGCCCATTTG AGGTCCTCT CACAGTGTCT CGTCTGTCTG TCCCTGTCTG GATGTCTGGA GTCGTCTGTG
151 V Q W K V D N A L Q S G N S Q E S V T E Q D S K D S T Y S L S S T

nmlI      maeIII bsaJI      maeIII      hglI
bslI      maeIII bsaJI      maeIII      hglI
4201 CTGACGCTGA GCRAAGCAGA CTACGAGAAA CACAAAGTCT ACGCTGCGA AGTCACCCAT CAGGCGCTGA GCTCGCCCTG CACAAAGAGC TTCAACAGGG
GACTGCGACT CGTTCTGTCT GATGCTCTTT GTGTTTCAGA TCGGAGCGCT TCAGTGGGTA GTCCCGGACT CGAGCGGGCA GTGTTCTCG AAGTTCTCCC
184 L T L S K A D Y E K H K V Y A C E V T H Q G L S S P V T K S F N R G

dclI      celII/espI      hglI      hphI      maeIII      aluI
blpI/bpuII102I      hglI      hphI      maeIII      aluI
4301 GAGAGTGTGA AGCTTGGCCG CCATGGCCCA ACTTGTTTAT TGCAGCTTAT AATGGTTACA AATAAGCAA TAGCATCACA AATTTCACA ATAAAGCATT
CTCTCACAAT TCGRACCGGC GGTACCGGT TGAACAAATA ACGTGGAATA TTACCAATGT TATTTCGT ATCGTAGTGT TTAAGTGT TATTTCGTAA
218 E C O (SEQ ID NO.72)

sau96I      acII      haeIII/palI
acII      fnu4HI      asuI
bsuI      nlaIII
sfII      styI
aluI      haeIII/palI
hindIII      bglI      ncoI
tru9I      eaeI      dsaI
mseI      cfrI      bsaJI
4301 GAGAGTGTGA AGCTTGGCCG CCATGGCCCA ACTTGTTTAT TGCAGCTTAT AATGGTTACA AATAAGCAA TAGCATCACA AATTTCACA ATAAAGCATT
CTCTCACAAT TCGRACCGGC GGTACCGGT TGAACAAATA ACGTGGAATA TTACCAATGT TATTTCGT ATCGTAGTGT TTAAGTGT TATTTCGTAA
218 E C O (SEQ ID NO.72)

```

FIG. 480

FIG. 48P

FIG. 48Q

FIG. 48B

101 0.0. FIG.

mspi nlaiv
hpaII hgiJII
nael bsp1286
cfr101/bsrFI bmyI
maeII cac8I aluI nlaiv
5301 TTTCTGCGCA CGTTCGCGG CTTTCCCGGT CAAGCTCTAA ATCCGGGGCT CCCTTTAGGG TTCCGATTTA GTGCTTTACG GCACCTCGAC CCCAAAAAAC
AAAGAGGGT GCAAGCGGC GAAAGGGGCA GTTCGAGATT TAGCCCCCGA GGGAAATCCC AAGGCTAAAT CACGAAATGC CGTGGAGCTG GGGTTTTTGG
maeII haeIII/palI
draIII sau96I
bpaII asuI
hphI
5401 TTGATTGGG TGATGGTTCA CGTACTGGG CATCGCCCTG ATAGACGGTT TTTGGCCCTT TGACGTTGGA GTCCACGTTT TTAATAGTG GACTCTTGT
AACTAAACCC ACTACCAAGT GCATCACCG GTAGCGGAC TATCTGCCAA AAGCGGAA ACTGCAACCT CAGGTGCAAG AAATTATCAC CTGAGAACAA
bslI
belI aval
brrI
5501 CCAAACTGGA ACAACACTCA ACCCTATCTC GGGCTATTCT TTTGATTAT AAGGGATTTT GCGATTTCG GCCTATTGGT TAAAAAATGA GCTGATTAA
GGTTTGACCT TGTGTGAGT TGGGATAGAG CCCGATAGA AACTAAATA TTCCCTAAA CGCTAAAGC CGGATAACCA ATTTTACT CGACTAAAT
tru9I maeII
hgiAI/aspHI
bspl286
bsiHKAI
bmyI ddelI
apaLI/snoI rsaI
alw41/snoI csp6I
5601 CAAAAATTTA ACAGGATTT TAACAAATA TTAACGTTTA CAATTTTATG GTGCACCTC AGTACAATCT GCTCTGTATG CGCATAGTTA AGCCAACTCC
GTTTTTAAAT TGCGCTTAA ATTGTTTAT AATTGCAAT GTTAAATATC CAGGTGAGAG TCATGTTAGA CGAGACTAGC GCGTATCAAT TCGGTTGAGG
thai
fnuDII/mvni
tru9I apoI tru9I
msei bstUI msei
apoI bsh1236I
5701 GCTATCGCTA CGTACTGGG TCATGCTGC GCCCGACAC CGCCGACAC CGCTGACG GCGTGTGTCG TCCCGCATC CGCTTACAGA
CGATAGCGAT GCACTGACCC AGTACCGACG CGGGGCTGTG GCGGCTGTG GCGGCTGCG CGGACTGCC CGAACAGAG AGGCGGTAG CGGAATGTCT
hinPI
hhal/cfoI
thai
fnuDII/mvni
bstUI
nspBII bsh1236I
acuI hgaI
acuI hgaI
5701 GCTATCGCTA CGTACTGGG TCATGCTGC GCCCGACAC CGCCGACAC CGCTGACG GCGTGTGTCG TCCCGCATC CGCTTACAGA
CGATAGCGAT GCACTGACCC AGTACCGACG CGGGGCTGTG GCGGCTGTG GCGGCTGCG CGGACTGCC CGAACAGAG AGGCGGTAG CGGAATGTCT

FIG. 48S

FIG. 48T

FIG. 48U

6601 CGACGAGCGT GACACCAGCA TGCAGCAGC AATGGCAGCA ACGTGGCGCA AACTATTAACT TGGCGAACTA CTTACTCTAG CTTCCCGGCA ACAATTAATA GCTGCTCGCA CTGTGGTGTG ACGTGTGTG TTAACCGCTT TGAACGCGT TGAATGATG ACGCTTGTG GAATGAGATC GAAGGGCGCT TGTTAATTAT

6701 GACTGGATGG AGGCGGATAA AGTTGCAGCA CCACTTCTGC GTCGGGCCCT TCCGGCTGGC TGGTTTATTG CTGATAAATC TGGAGCCGGT GAGCGTGGGT CTGACCTACC TCCGCCATT TCAACGTCTT TCAACGTCTT GGTGAAGACG CGAGCCGGGA AGGCCGACCG ACCAATAAC GACTATTAG ACCTCGGCCA CTGCGACCCA

6801 CTCGGCGTAT CATTTGACCA CTGGGGCCAG ATGGTAAGCC CTCGGTATCT GTAGTTATCT ACACGACGGG GAGTCAGGCA ACTATGGAT AACGAAATAG GAGCGCATTA GTAACGTGCT GACCCCGGTC TACCATTGGG GAGCGCATAG CATCAATAGA TGTGCTGCC CTCAGTCCGT TGATACCTAC TTGCTTTATC

6901 ACAGATCGCT GAGATAGGTC CCTCACTGAT TAAGCACTGG TAACGTGTCAG ACCAAGTTTA CTCATATATA CTTTAGATTG ATTTAAACT TCATTTTAA TGTCTAGCGA CTCTATCCAC GGAGTGACTA ATTCGTAAAC ATTGACAGTC TGGTTCAAAT GAGTATATAT GAAATCTAAC TAAATTTTGA AGTAAAAAT

7001 TTTAAAGCA TCTAGGTGAA GATCCTTTTT GATAATCTCA TGACCAAAAT CCCTTAACGT GAGTTTTCGT TCCACTGAGC GTCAGACCCC GTAGAAAAGA AAATTTTCT AGATCCACT CTAGGAAAAA CTATTAGAT ACTGGTTTTA GGGAAATGCA CTTCAAGCA AGGTGACTCG CAGCTGGG CATCTTTCT

FIG. 48V

[illegible]

FIG. 48W

FIG. 48X

FIG. 48Y

```

thai
fnuDI1/mvni
bstUI
bsh1236I
hinPI
hhal/cfoI
thai
fnuDI1/mvni
bstUI haeIII/palI
bsh1236I
mnlI
acII
7901 CCGCCTCTCC CCGCGCGTTG GCGGATTAT TAATCCAGCT GGCAGACAG GTTCCCGAC TGGAAAGCGG GCAGTGAGCG CAACGCAATT AATGTGAGTT
GGCGGAGAGG GGCGCGCAAC CGGCTAAGTA ATTAGGTCA CCGTCTGTC CAAAGGGGTG ACCTTTCGCC CGTCACTCGC GTTCCGTTAA TTACACTCAA
cac8I
alul
pvuII
tfII aseI/asnI/vsPI
hinPI
hhal/cfoI
msei
maeIII
tru9I
cac8I
acII
bseI
bsrI
cac8I
acII
bseI
bsrI
mspI
hpaII
nlaIV betNI
hgiCI apyI[dcmt+]
banI bsaJI
8001 ACCTCACTCA TTAGGCACCC CAGGCTTTAC ACTTTATGCT TCCGGCTCGT ATGTTGTGTG GAATTGTGAG CGGATAACAA TTTCACACAG GAAACACGTA
TGGAGTGAGT AATCCGTGGG GTCCGAAATG TGAATATCGA AGGCCGAGCA TACAACACAC CTTAACACTC GCCTATGTT AAAGTGTGTC CTTTGTGAT
acII
alul

```

FIG. 48Y

T E 6 3 0 " 3 3 2 3 6 0

tru9I
msel
aseI/asnI/vsPI
xmnl
nlaIII
asp700
8101 TGACCATGAT TACGAATTAA (SEQ ID NO.68)
ACTGGTACTA ATGCTTAATT

>length: 8120

aatII(GACGTC): 1690 5947
acc65I(GGTACC): 2969 3967 4529
accI(GTAKAC): 823 1039 2738 4237
aciI(CCGC): 217 229 238 250 260 271 317 422 454 485 574 1385 1795 1871 2248 2250 2758 2982
3167 3179 3188 3200 3210 3221 3267 3372 3404 3449 3686 3949 4021 4318 4542 4727
4739 4748 4760 4770 4781 4827 4910 4914 5070 5127 5153 5166 5203 5217 5220 5248
5275 5680 5699 5741 5751 5790 5979 6026 6125 6234 6311 6355 6476 6522 6713 6804
7166 7175 7310 7420 7541 7560 7687 7715 7806 7827 7834 7877 7901 7911 7967 8070
see hinII
acyI
afIII/bfII(CTTAAG): 786
afIII(ACRYGT): 932 7758
ageI(ACCGGT): 1833
ahaiI/baaiI(GRCGYC): 988 1690 1858 5117 5947 6329
ahaiI/drai(TTTAAA): 696 4935 6290 6982 7001
ahdi/eamII05I(GACNNNNNGTC): 2087 6865
alul(AGCT): 5 44 332 386 390 753 1097 1165 1370 1431 1951 2603 2751 2784 3282 3336 3340
3562 3566 3676 3733 3792 4270 4288 4311 4344 4554 4842 4896 4954 5047 5333 5590
5803 5822 6516 6579 6679 7200 7457 7593 7819 7937 8096
alw44I/snoI(GTGCAC): 1876 5651 6198 7444

FIG. 48Z

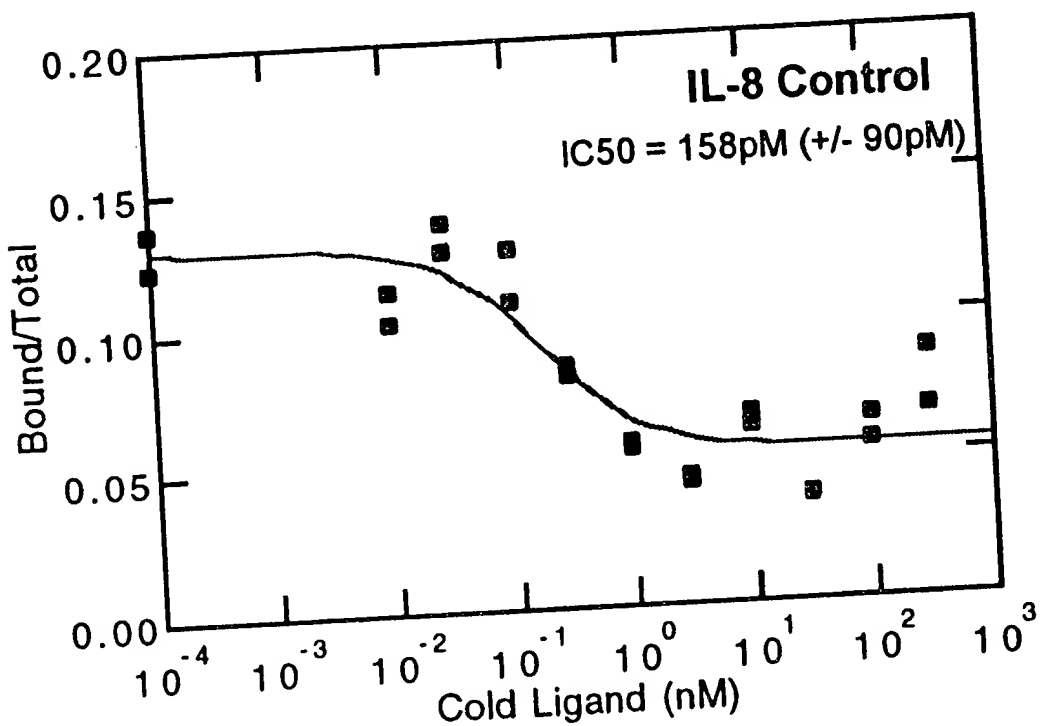


FIG. 49A

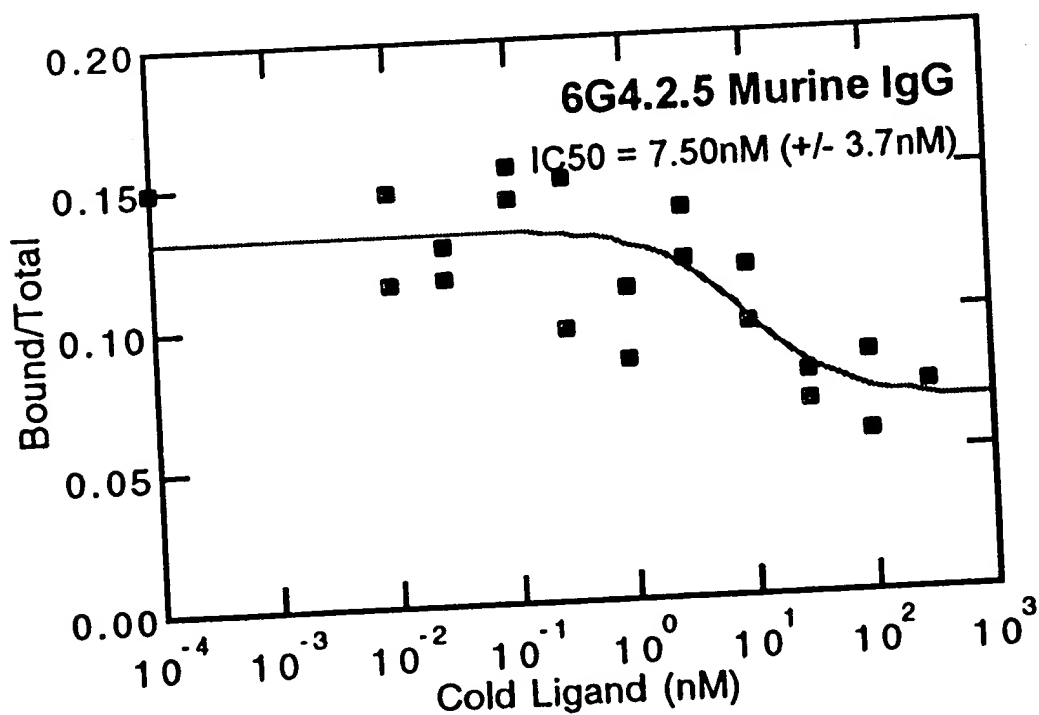


FIG. 49B

REF ID: A66325

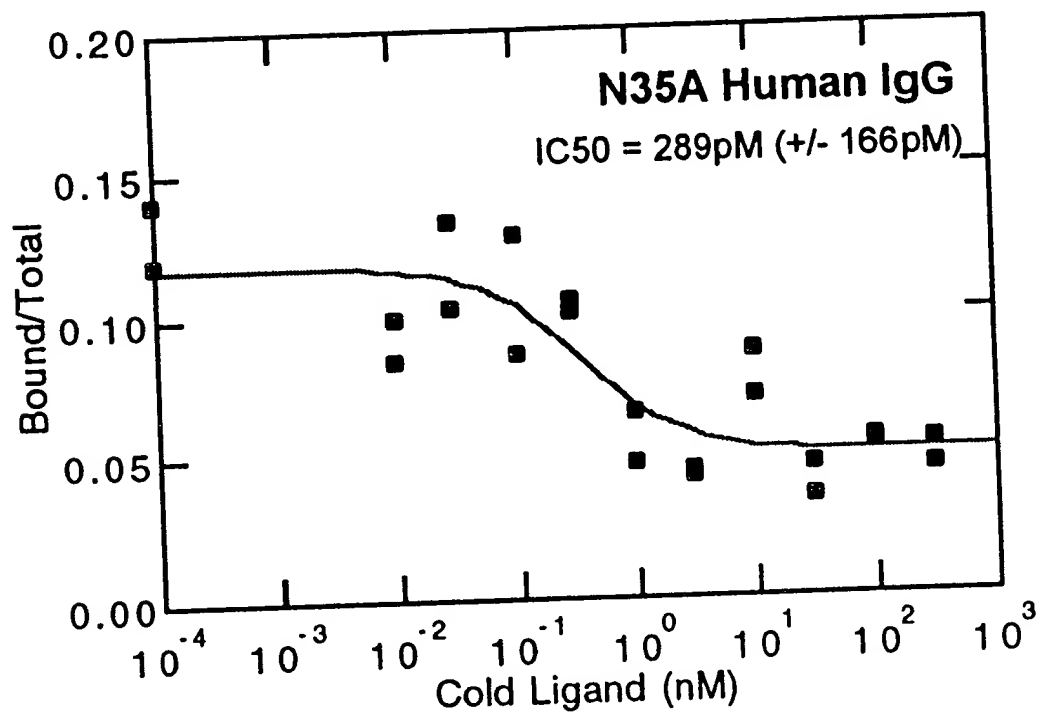


FIG. 49C

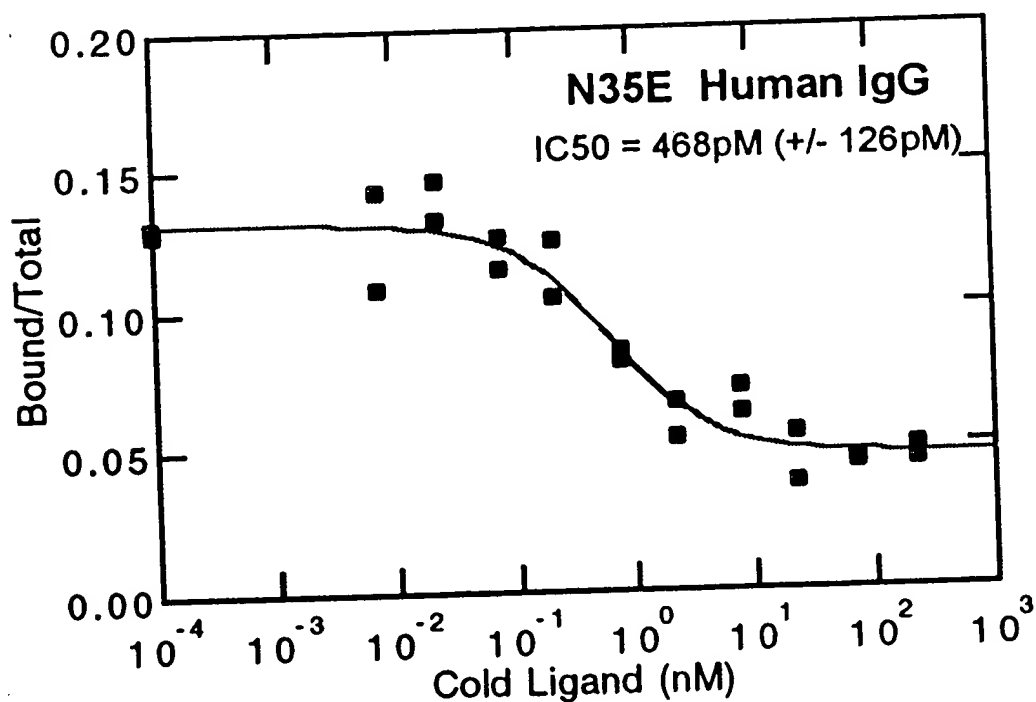


FIG. 49D

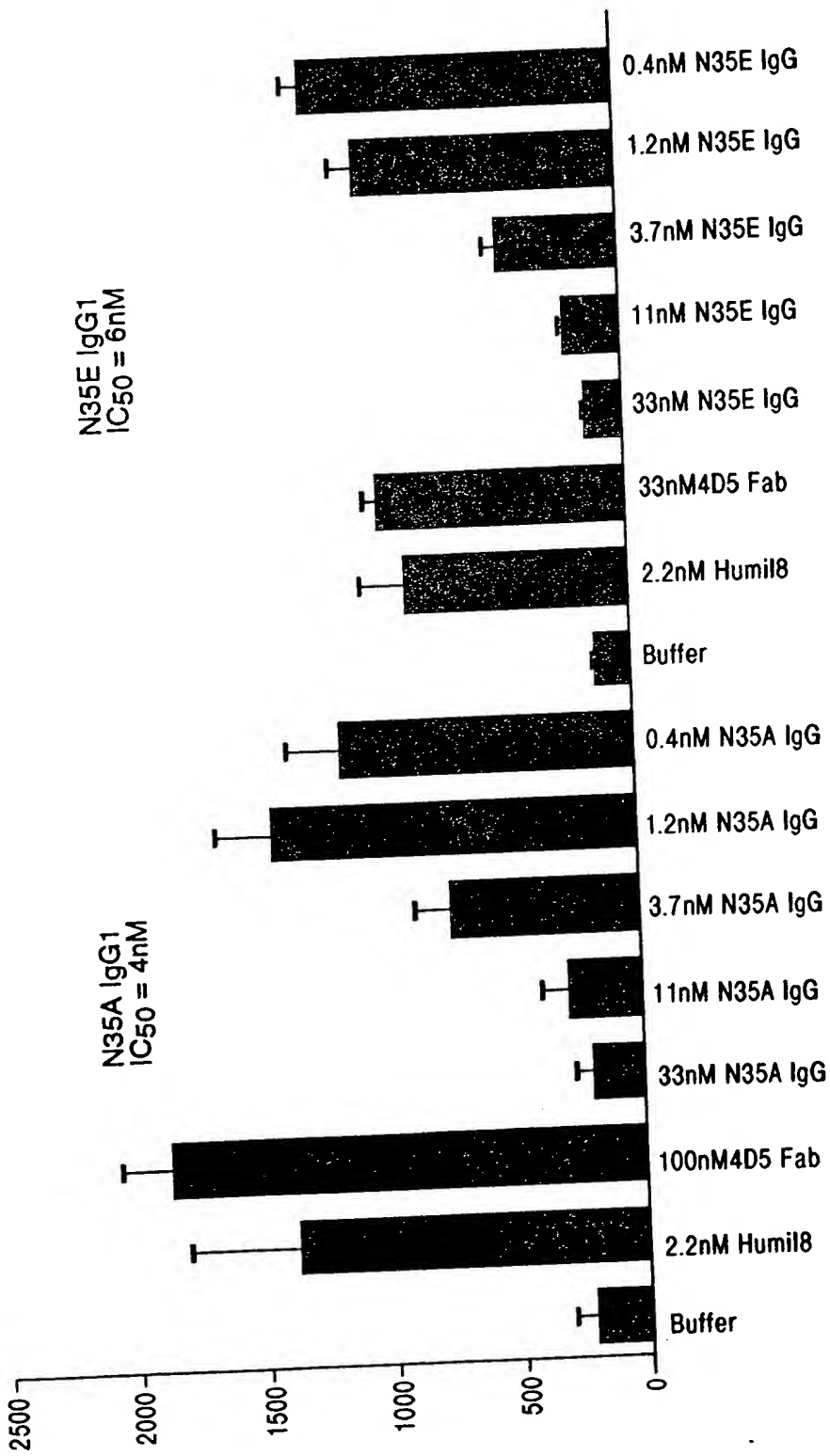


FIG. 50A

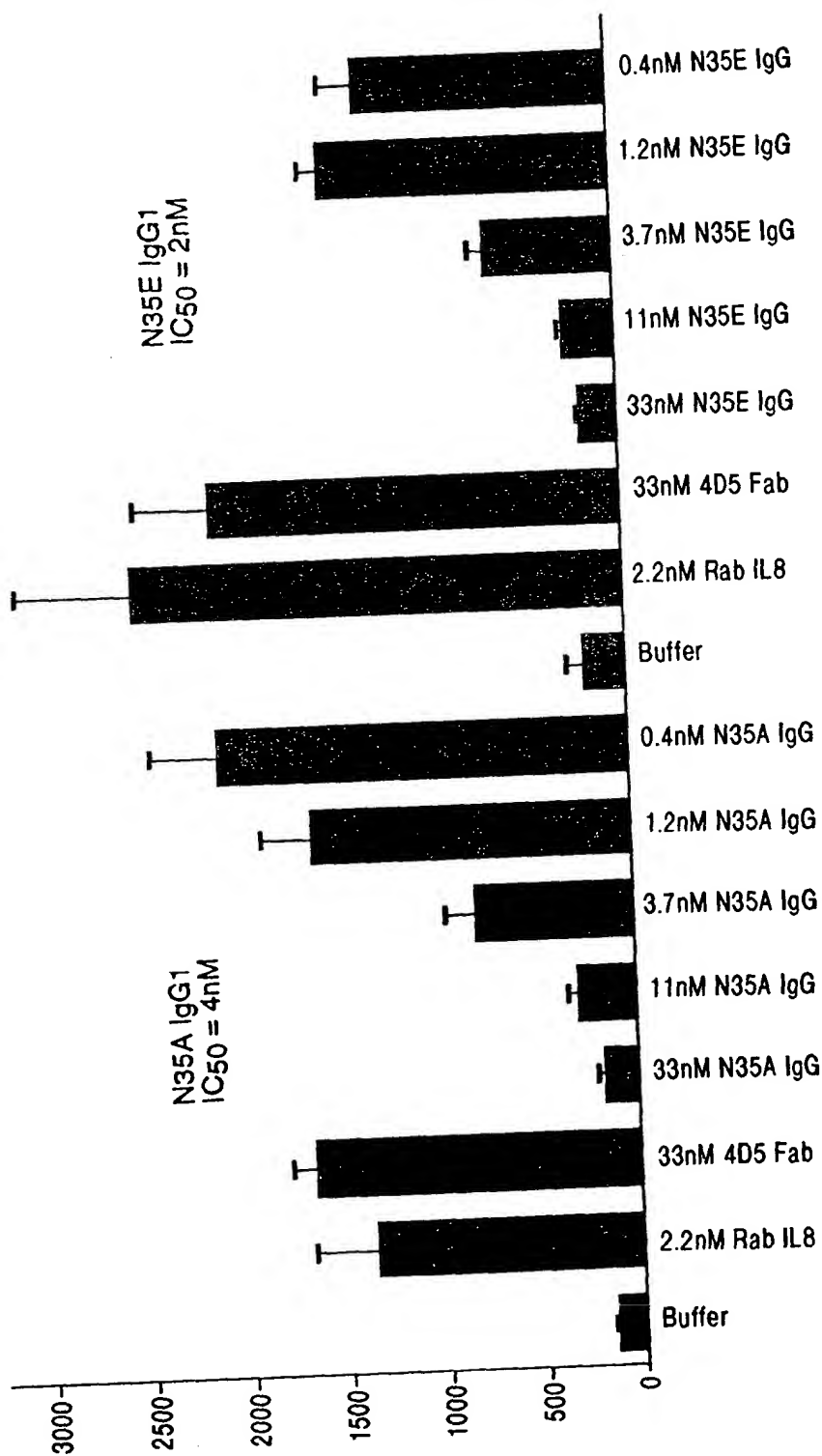


FIG. 50B



SAMPLE	ka	kd	Kd
Murine 6G4.2.5 IgG2a	8.3×10^5	2.9×10^{-4}	350pM
6G4V11N35A-IgG1	8.7×10^5	7.7×10^{-5}	88pM
6G4V11N35E-IgG1	3.0×10^6	1.4×10^{-4}	49pM

FIG. 51

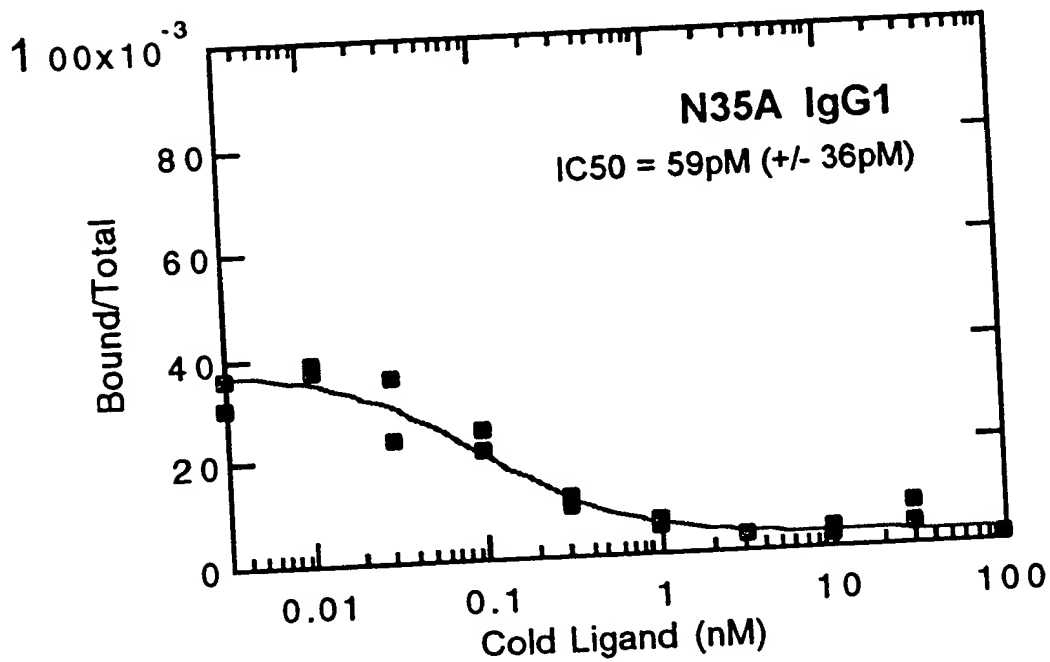


FIG. 52A

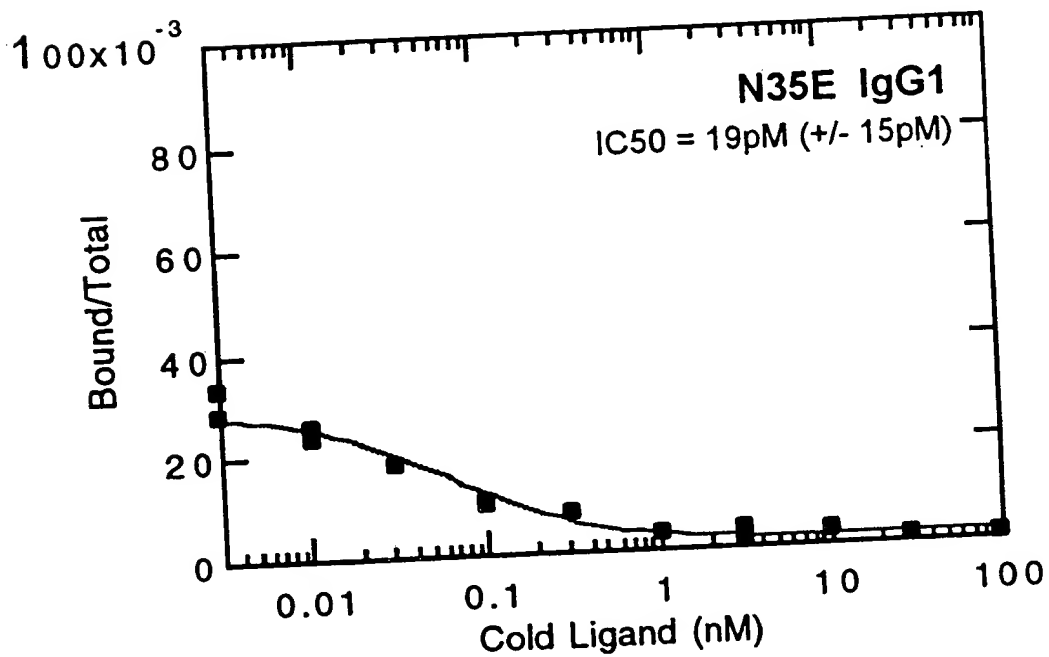


FIG. 52B

781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
 TTTTCCCATG GATCTCCAAC TCCACTAAAA TACTTTTTCT TATAGCGTAA AGAAGAACGT
 -1 M K K N I A F L L A

841 TCTATGTTCTG TTTTCTCTAT TGCTACAAAC GCGTACGCTG AGGTTCAGCT AGTGCAGTCT
 AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
 -11 S M F V F S I A T N A Y A E V Q L V Q S

901 GGCGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
 CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG
 8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCACATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCTGGAATGG
 AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTCCC GGACCTTACC
 28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
 CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTTCAA GTTCCCGGCA
 48 V G Y I D P S N G E T T Y N Q K F K G R

1081 TTCACTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
 AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA
 68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCCGTCTA TTAAGTGACA AGAGGGGATT ATCGCTACAA TGGTGACTGG
 CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCTTAA TAGCGATGTT ACCACTGACC
 88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
 AAGAAGCTGC AGACCCCACT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG
 108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
 GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGGTG TCGCCGGGAC
 128 P S V F P L A P S S K S T S G G T A A L

1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
 CCGACGGACC AGTTCTGTAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
 148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGCACAC CTTCCCCGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC
 GACTGGTTCG CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCTGA GATGAGGGAG
 168 L T S G V H T F P A V L Q S S G L Y S L

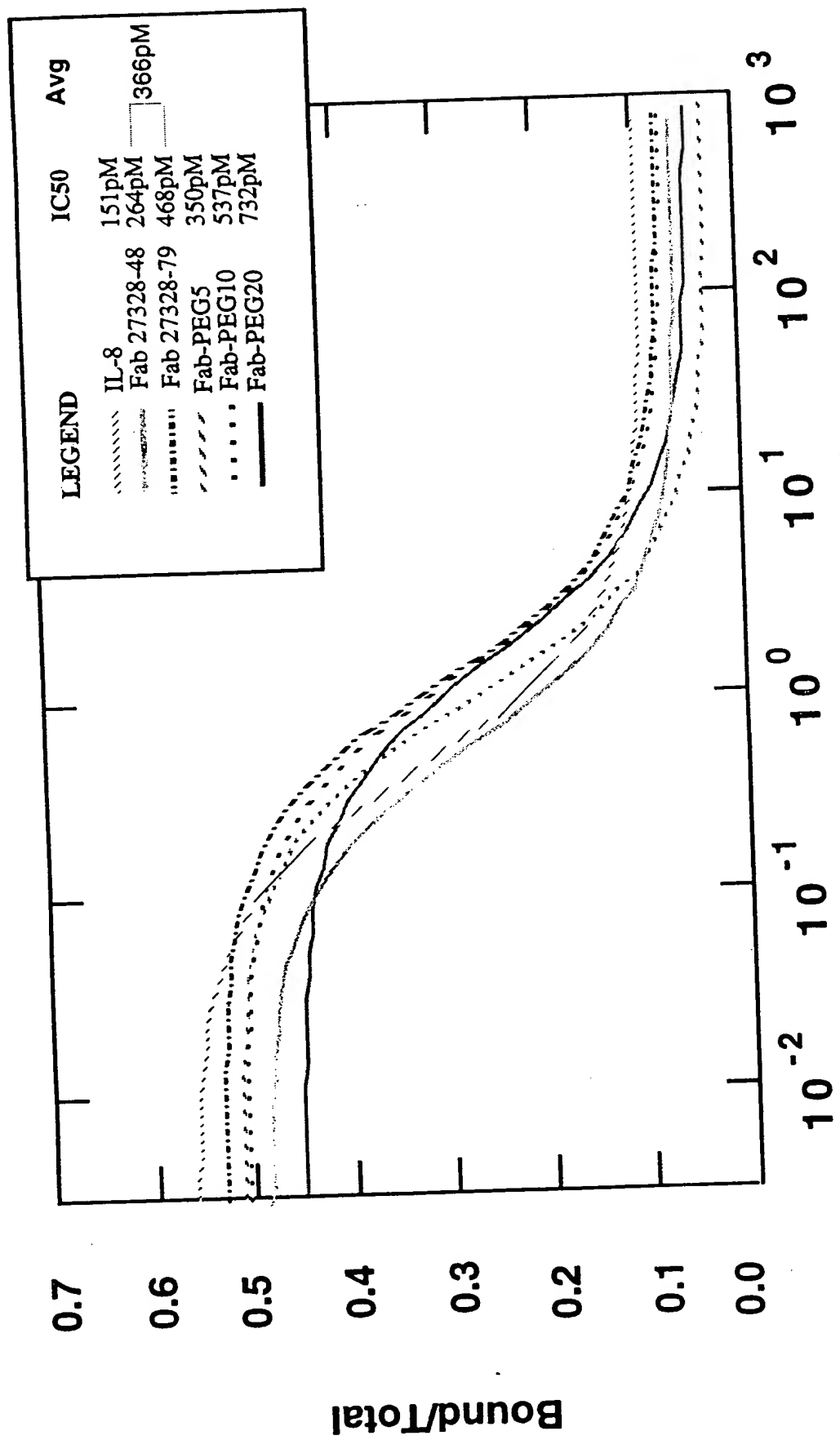
1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
 TCGTCGCACC ACTGGCACGG GAGGTGCTCG AACCCTGGG TCTGGATGTA GACGTTGCAC
 188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAGC CCAGCAACAC CAAGGTCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
 TTAGTGTTCTG GGTCTGTTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
 208 N H K P S N T K V D K K V E P K S C D K

1561 ACTCACACAT GCGCGCCGTGA (SEQ ID NO.69)
 TGAGTGTGTA CGGGCGGCACT
 228 T H T C P P O (SEQ ID NO.70)

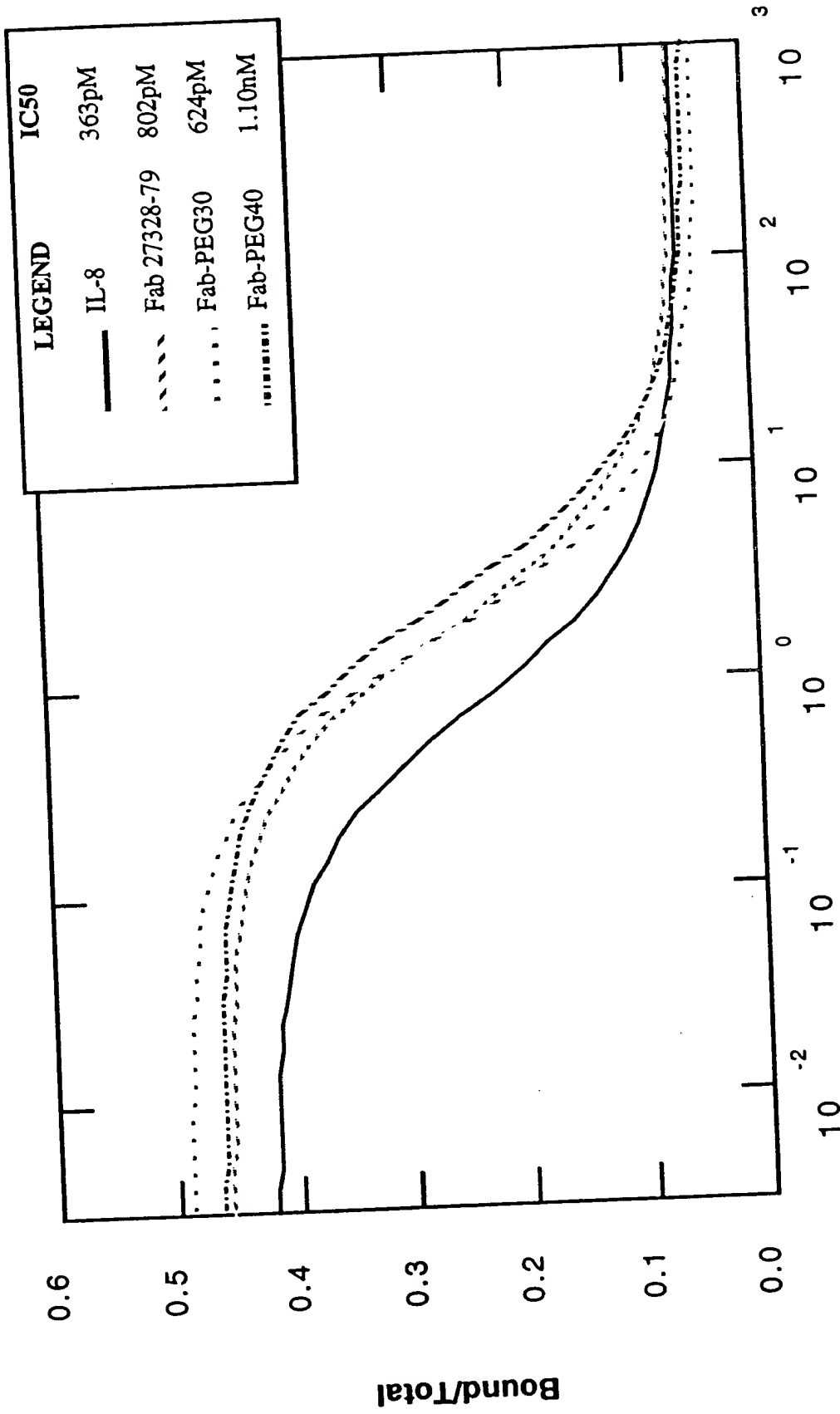
FIG. 53

REF ID: A66666



Antibody Competitor (nM)
 FIG. 54A

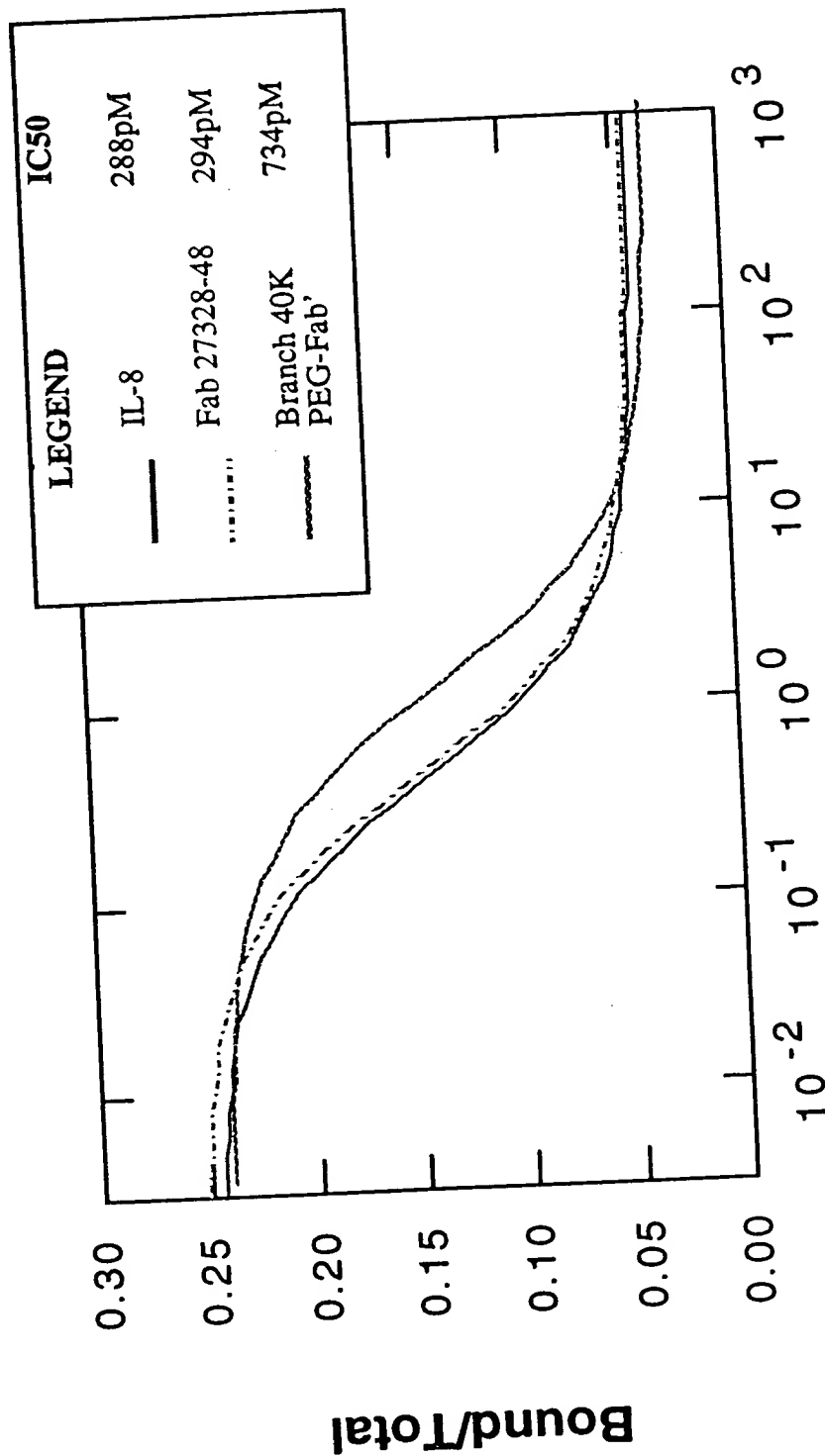
FIG. 54B



Antibody Competitor (nM)

FIG. 54B

FIG. 54C



Antibody Competitor (nM)

FIG. 54C

2003-03-20

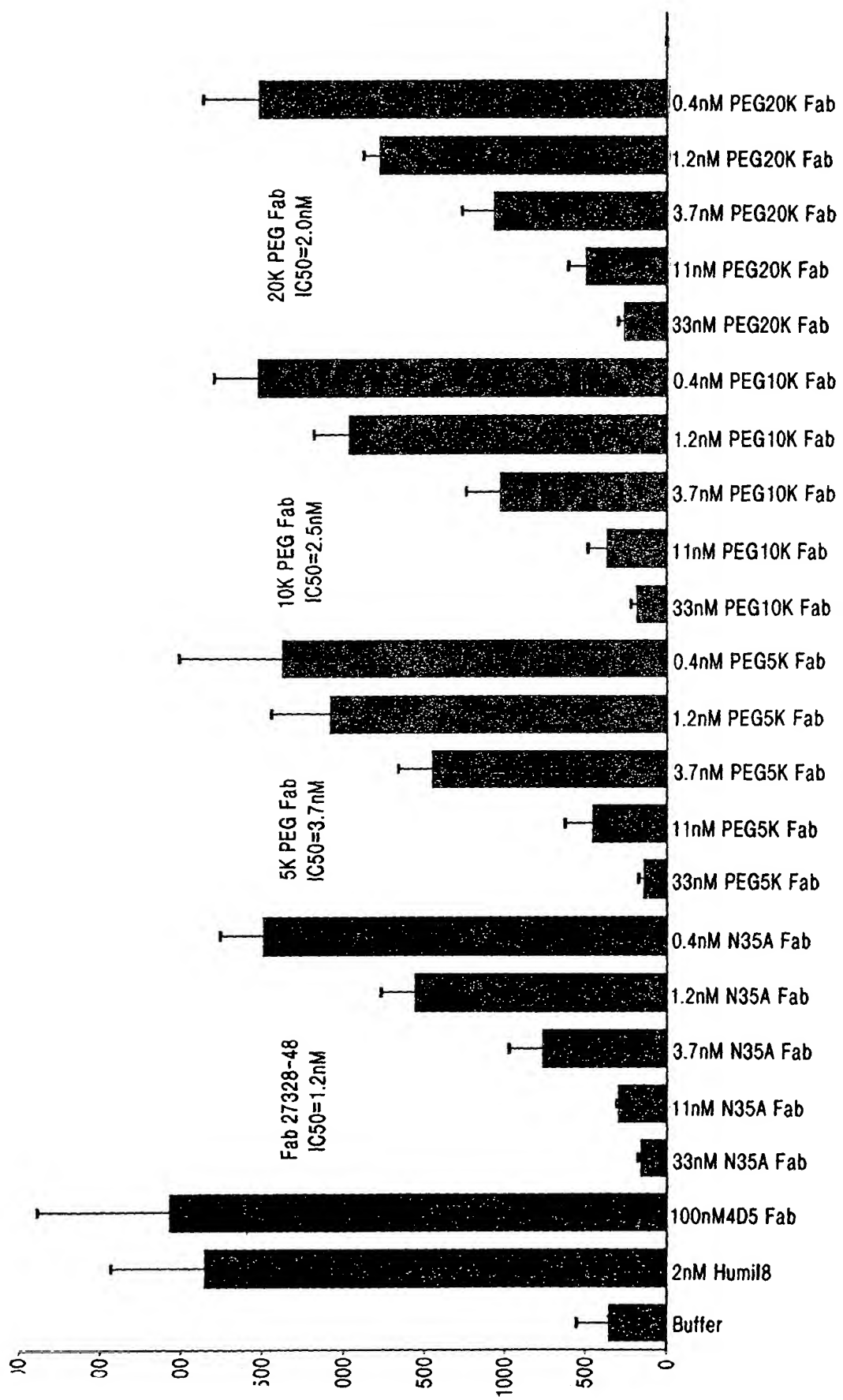


FIG. 55A

FIG. 55B

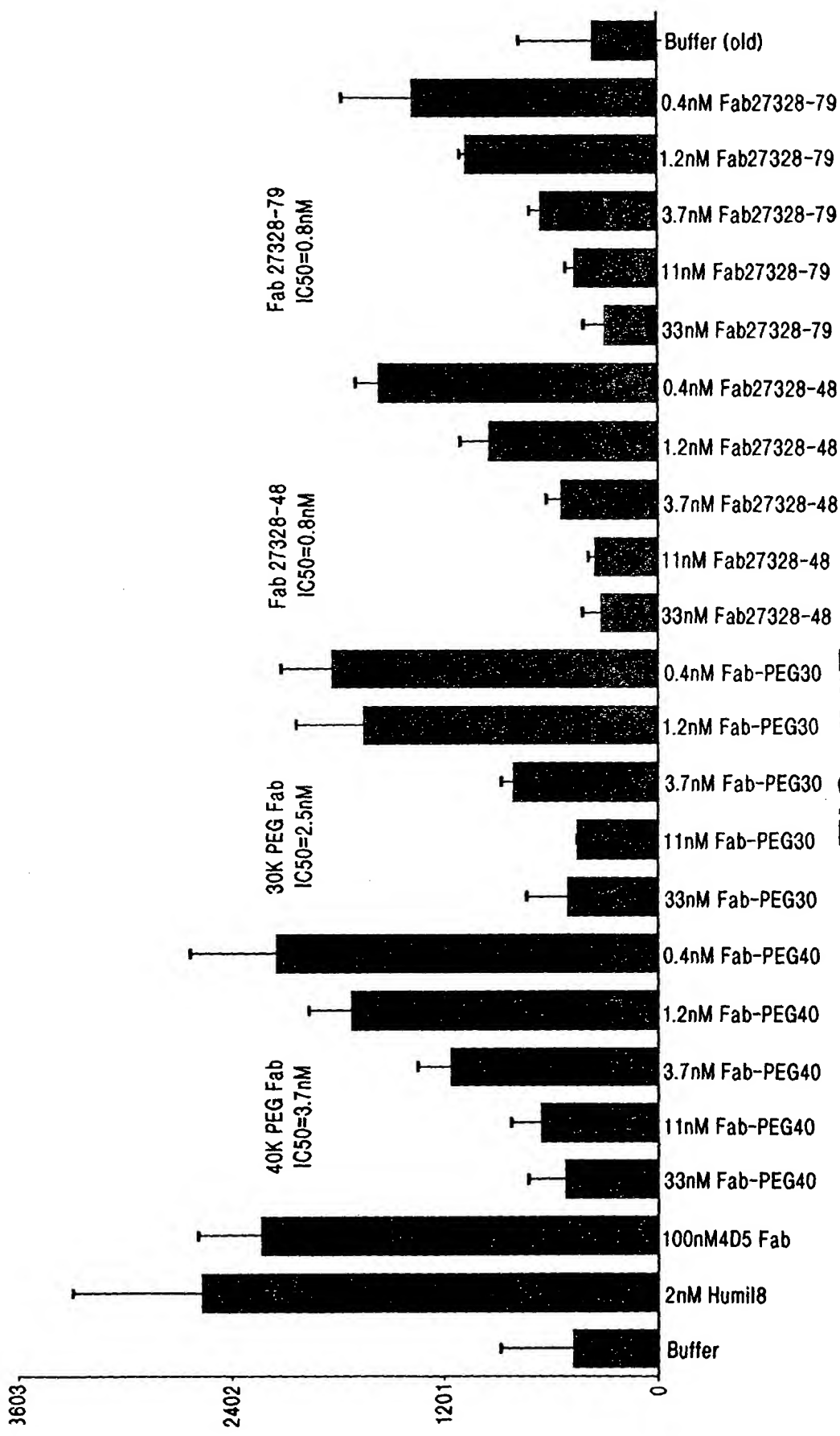


FIG. 55B

FIG. 55C

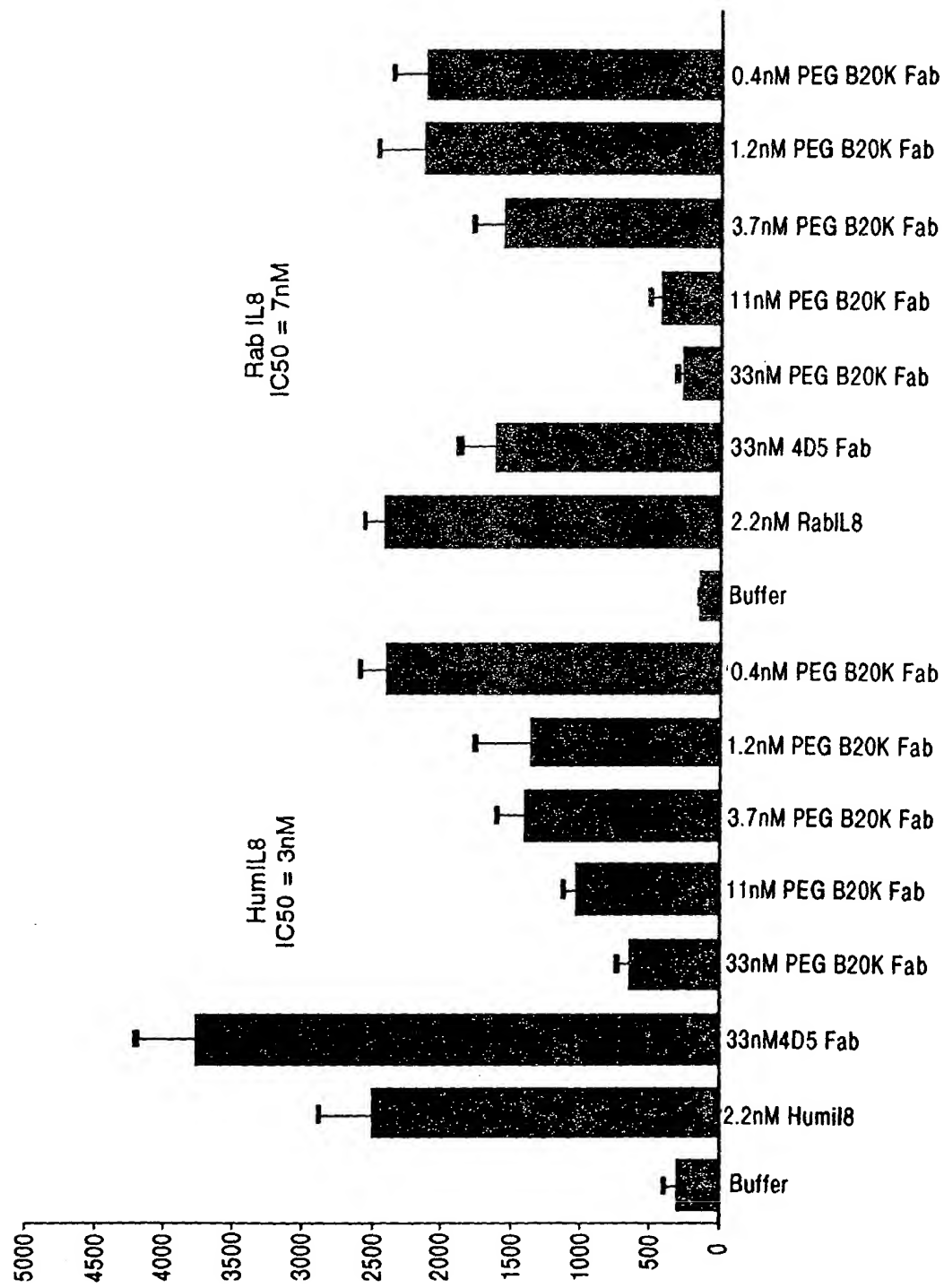
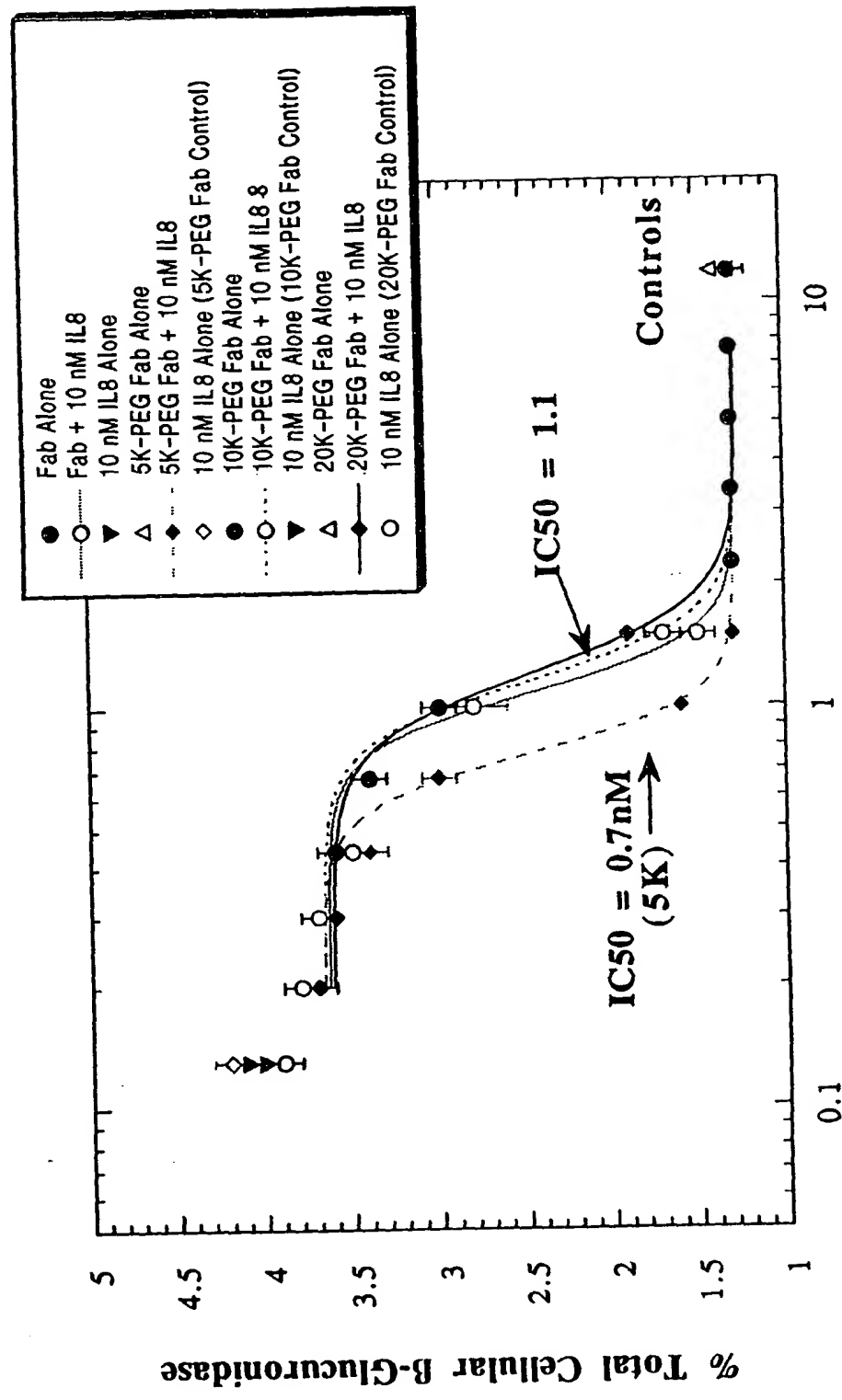


FIG. 55C

TOP SECRET 33266



Molar Ratio Antibody:IL-8

FIG. 56A

TOP SECRET 000000000000

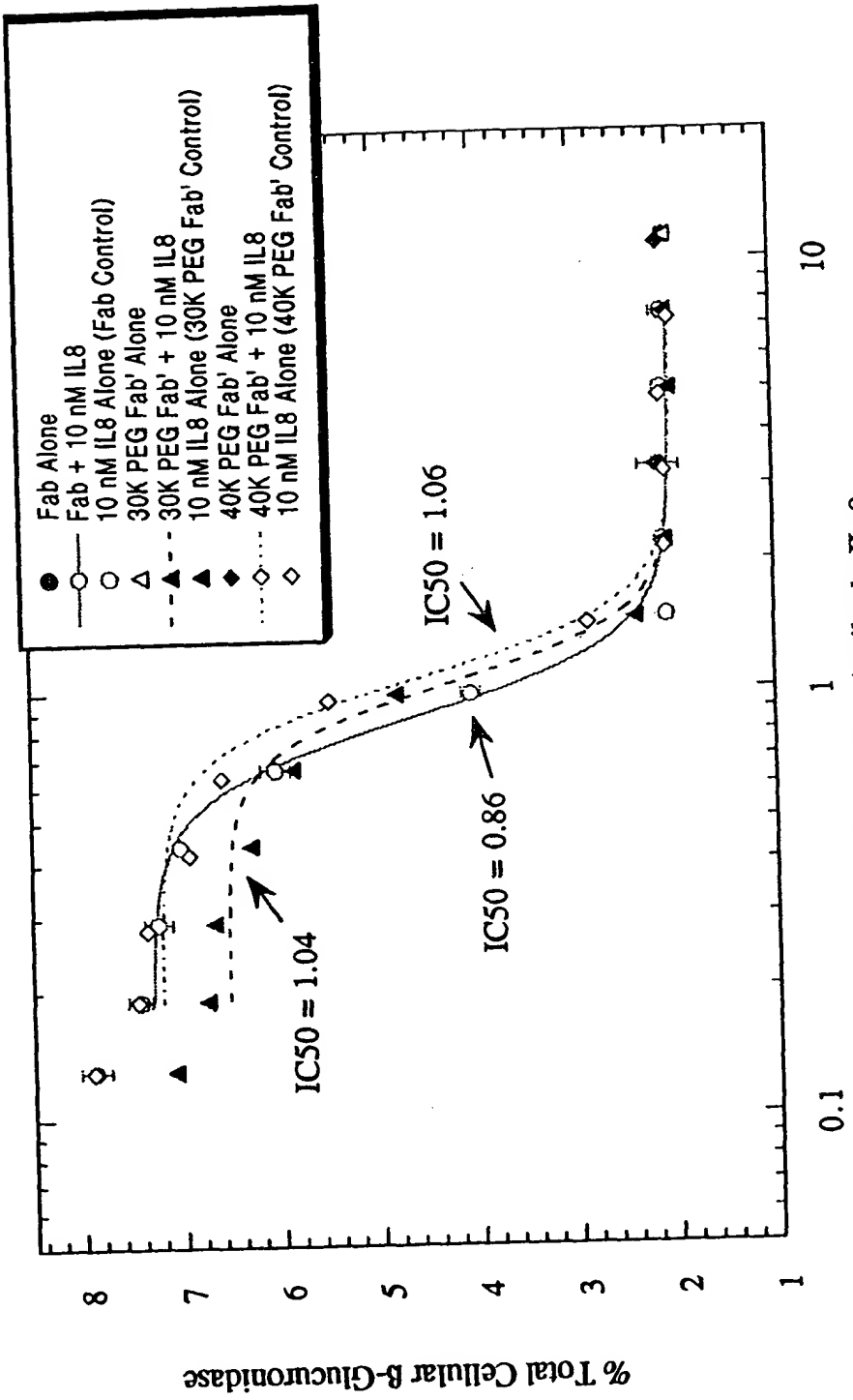
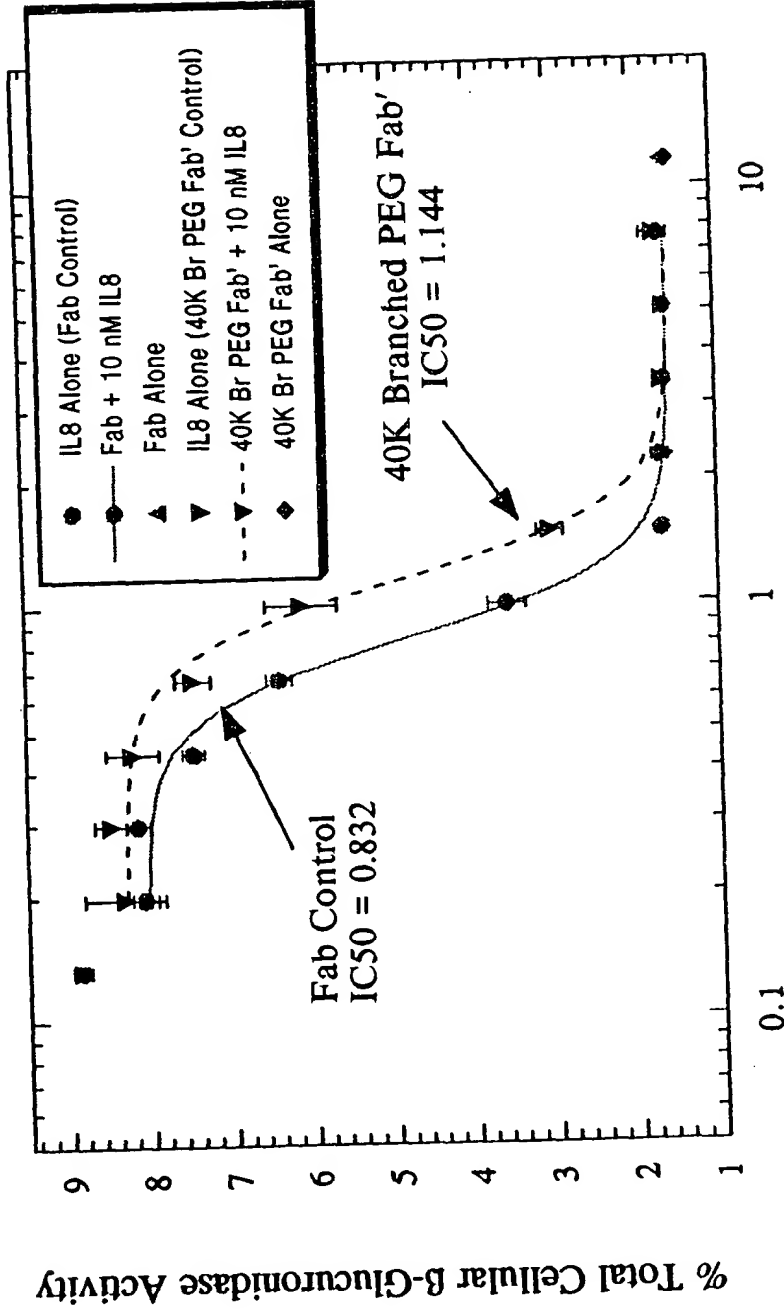


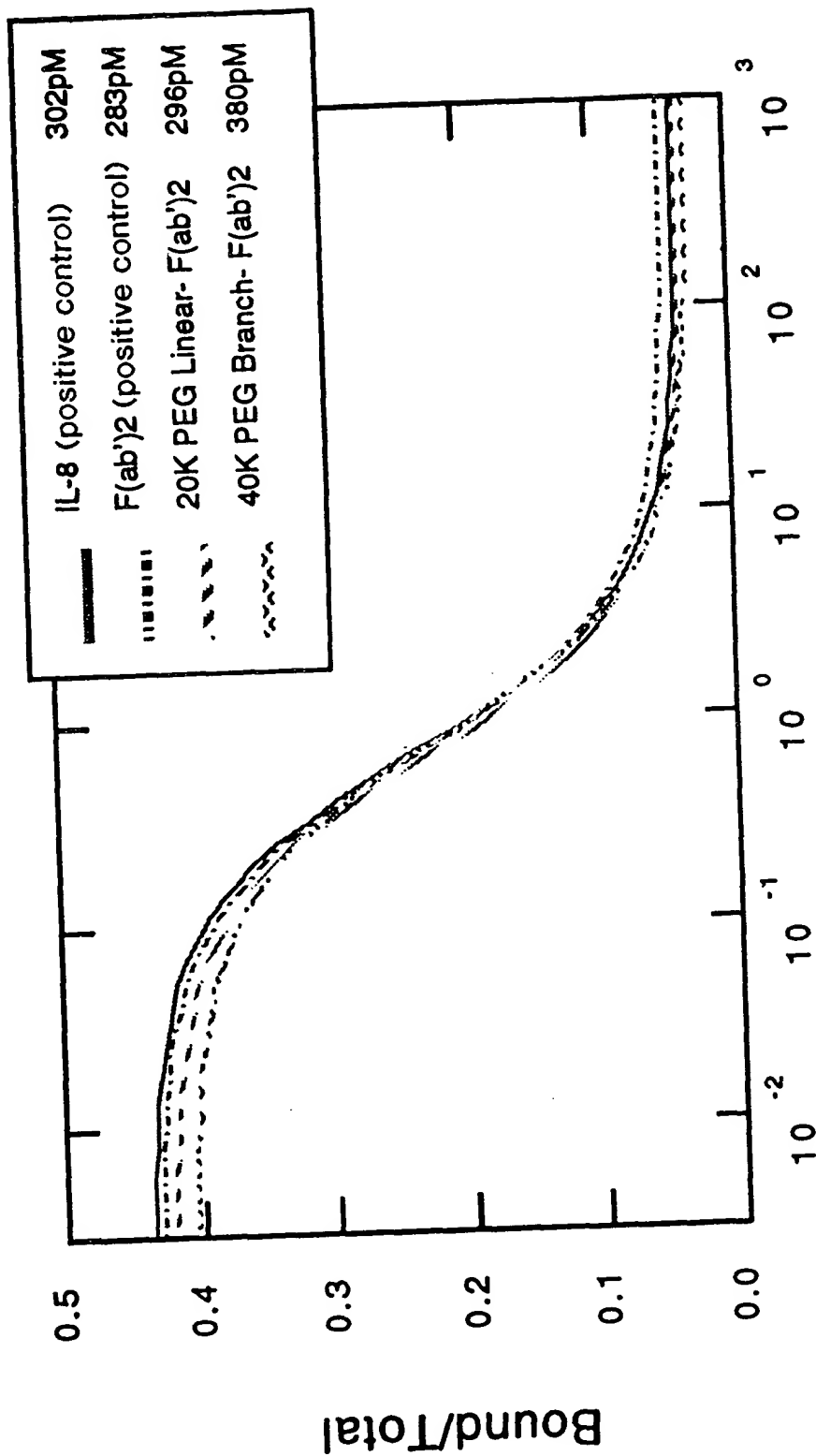
FIG. 56B



Molar Ratio Antibody:IL8

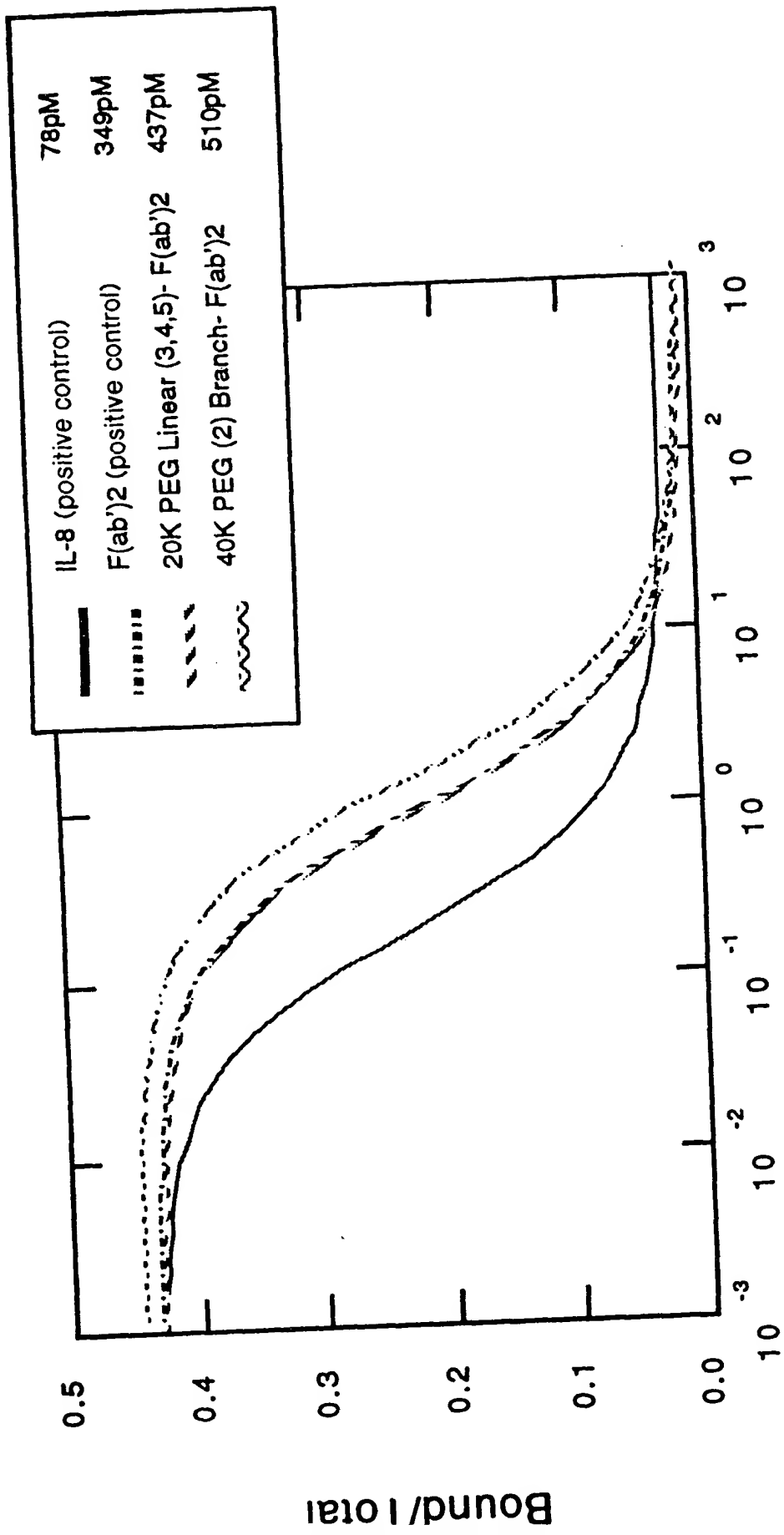
FIG. 56C

TOP SECRET



Pegylated F(ab')₂ (nM)

FIG. 57A



Pegylated F(ab')₂ (nM)

FIG. 57B

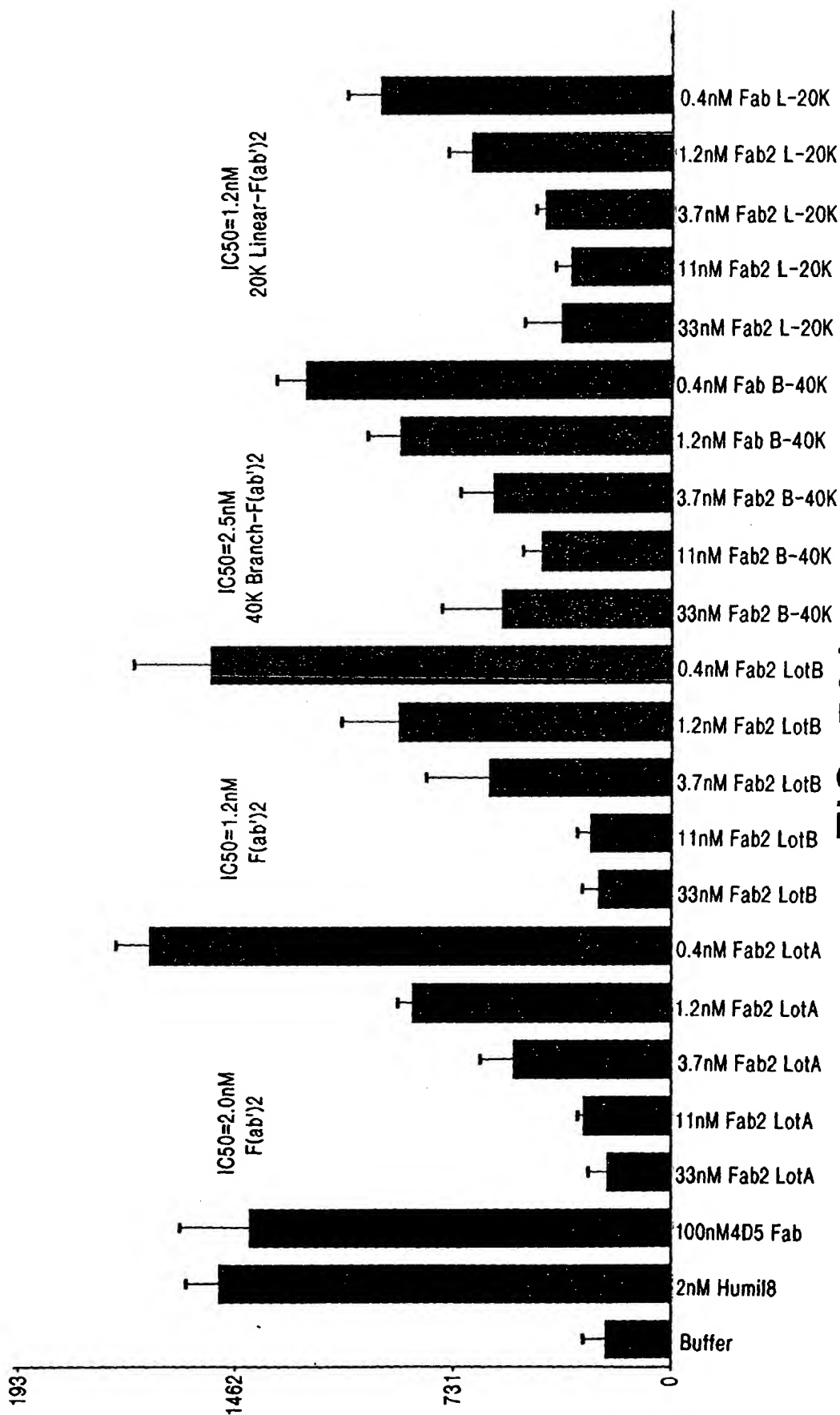


FIG. 58A

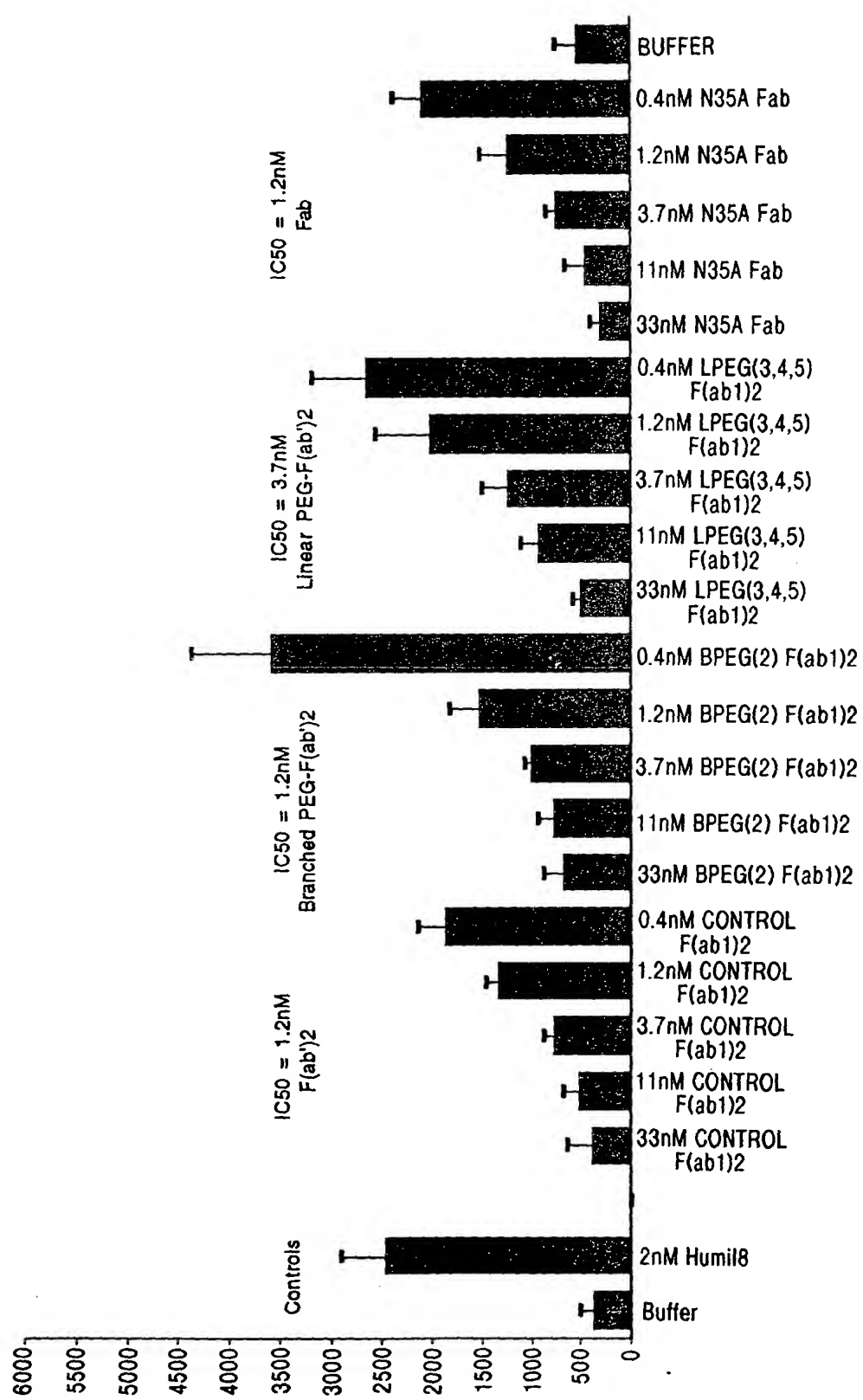
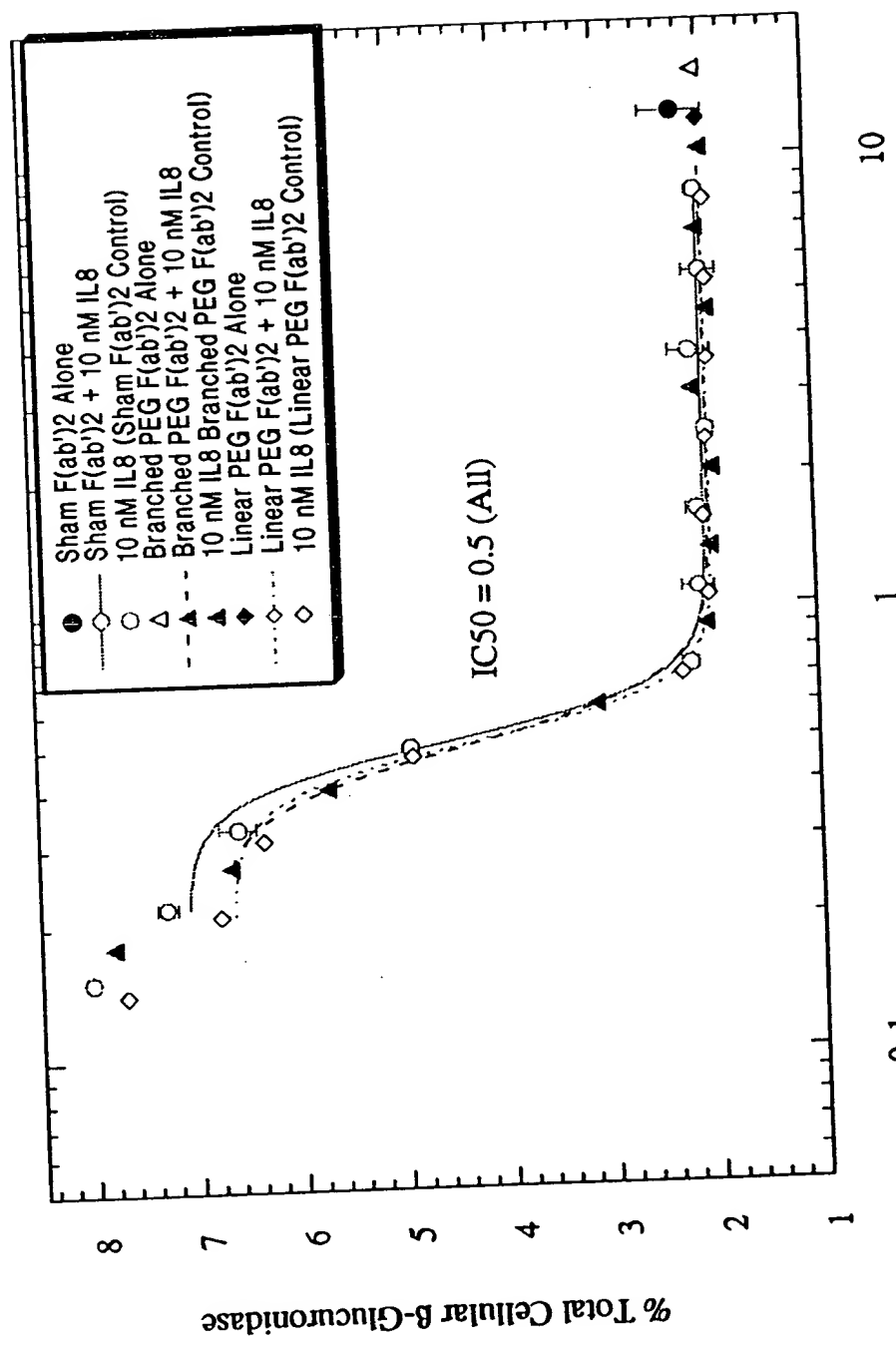


FIG. 58B



Molar Ratio Antibody:IL-8

FIG. 59A

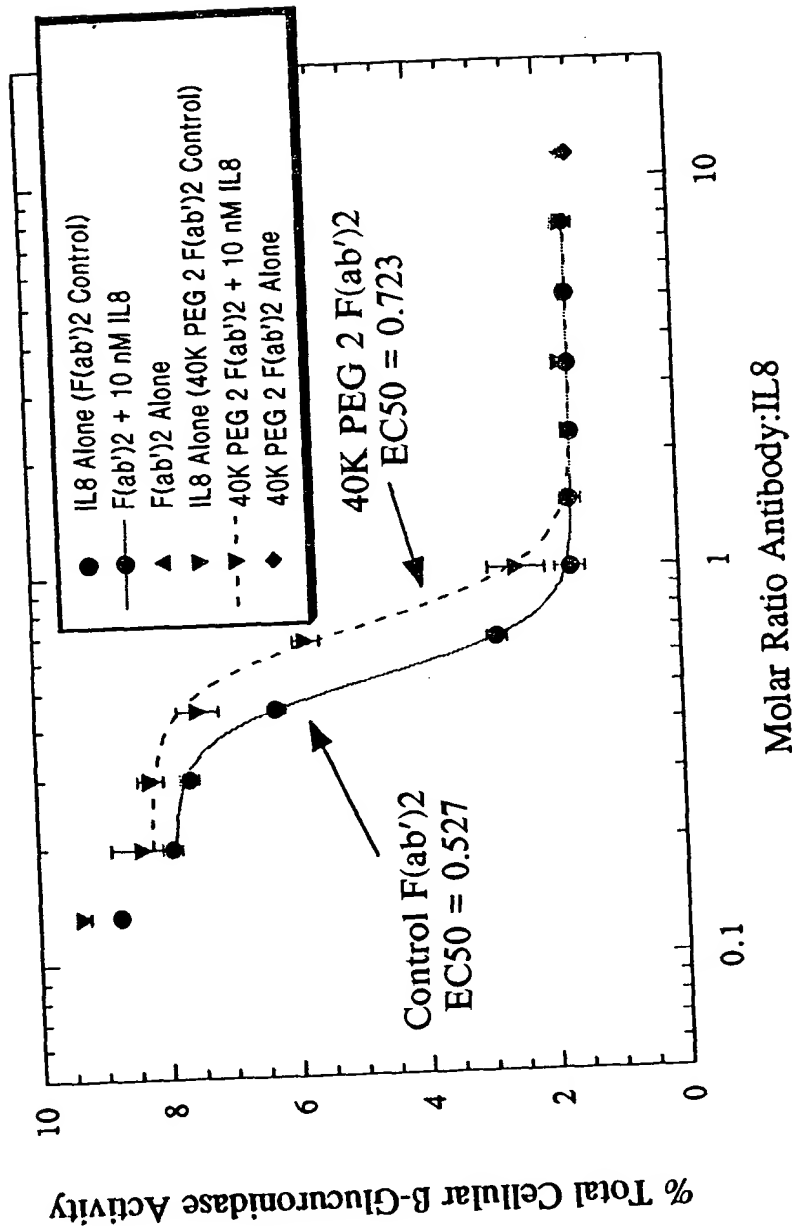
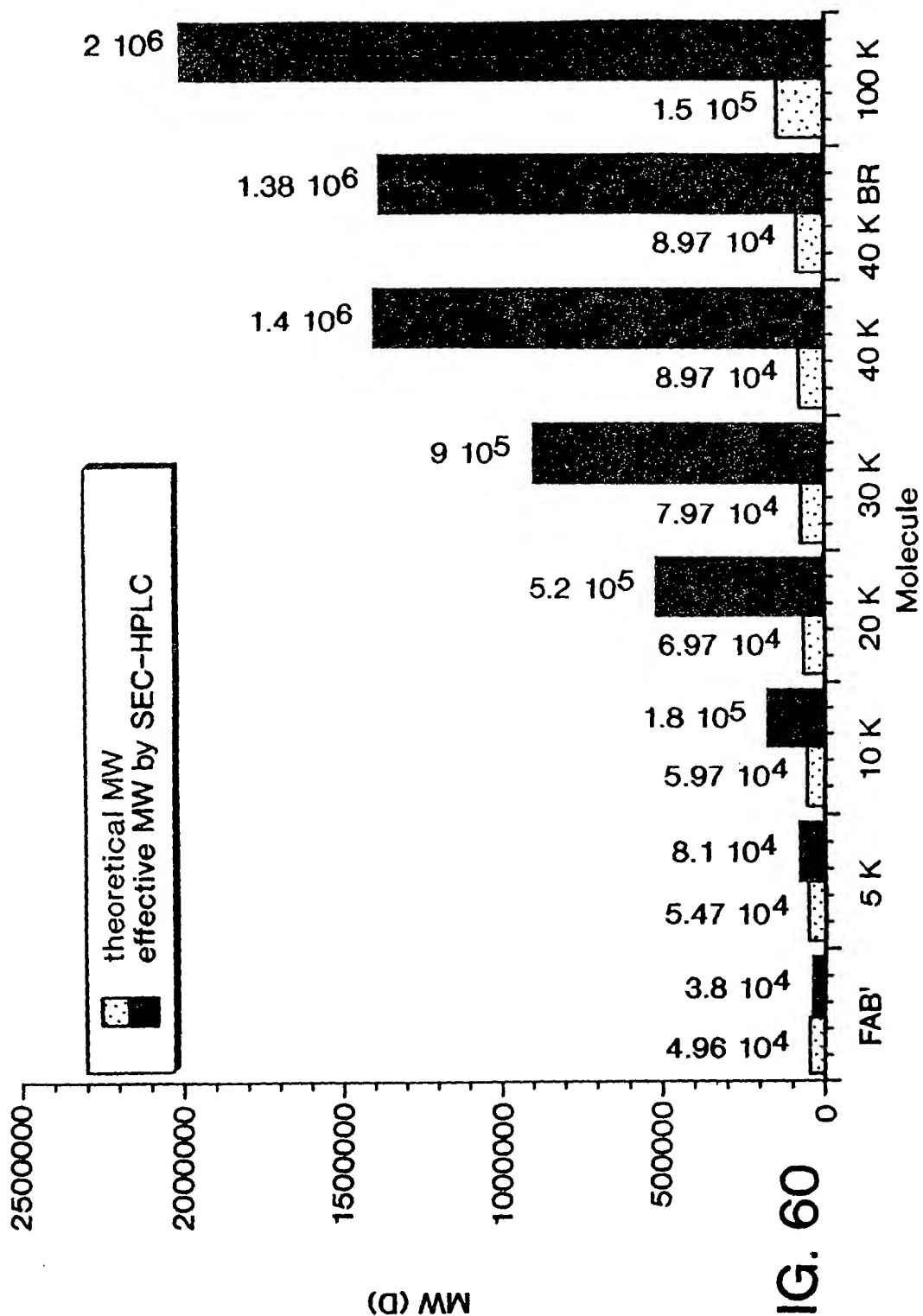
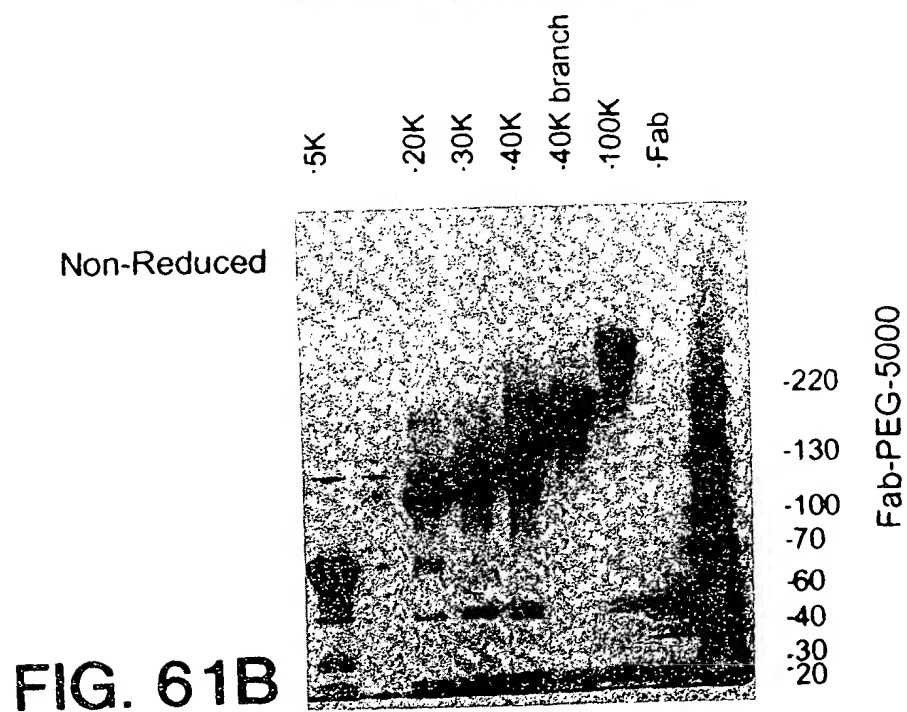
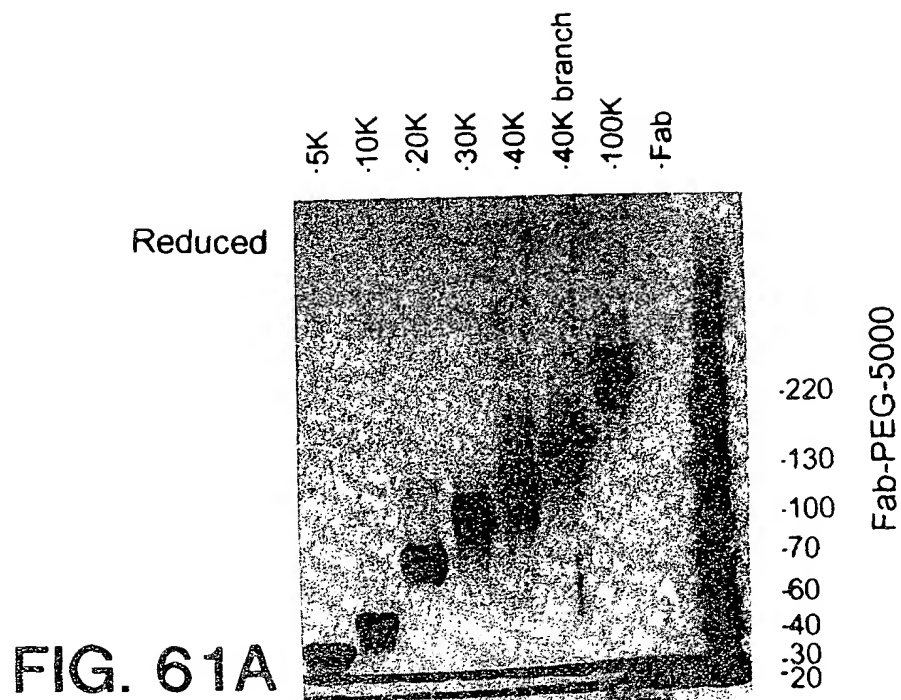


FIG. 59B





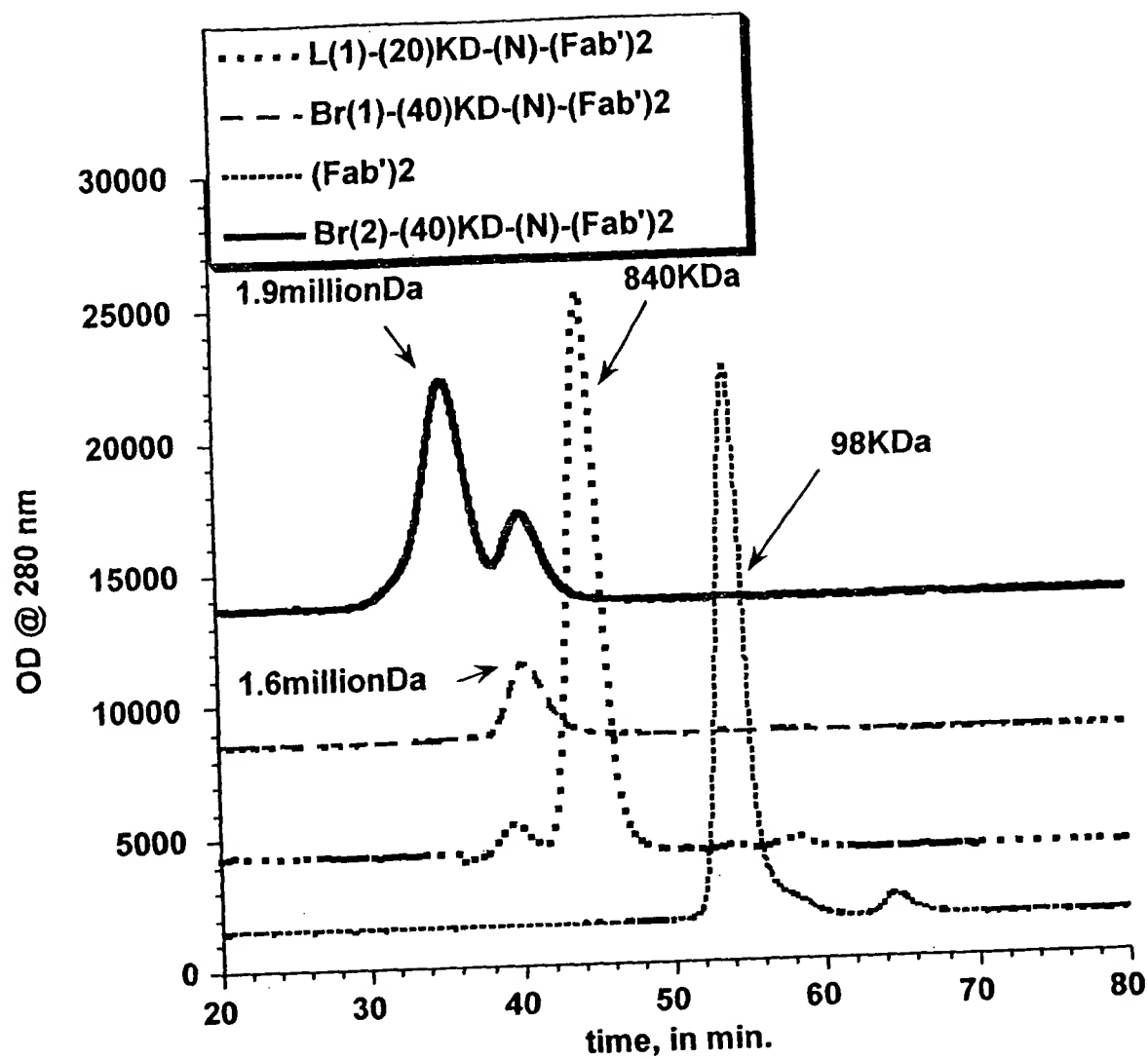


FIG. 62

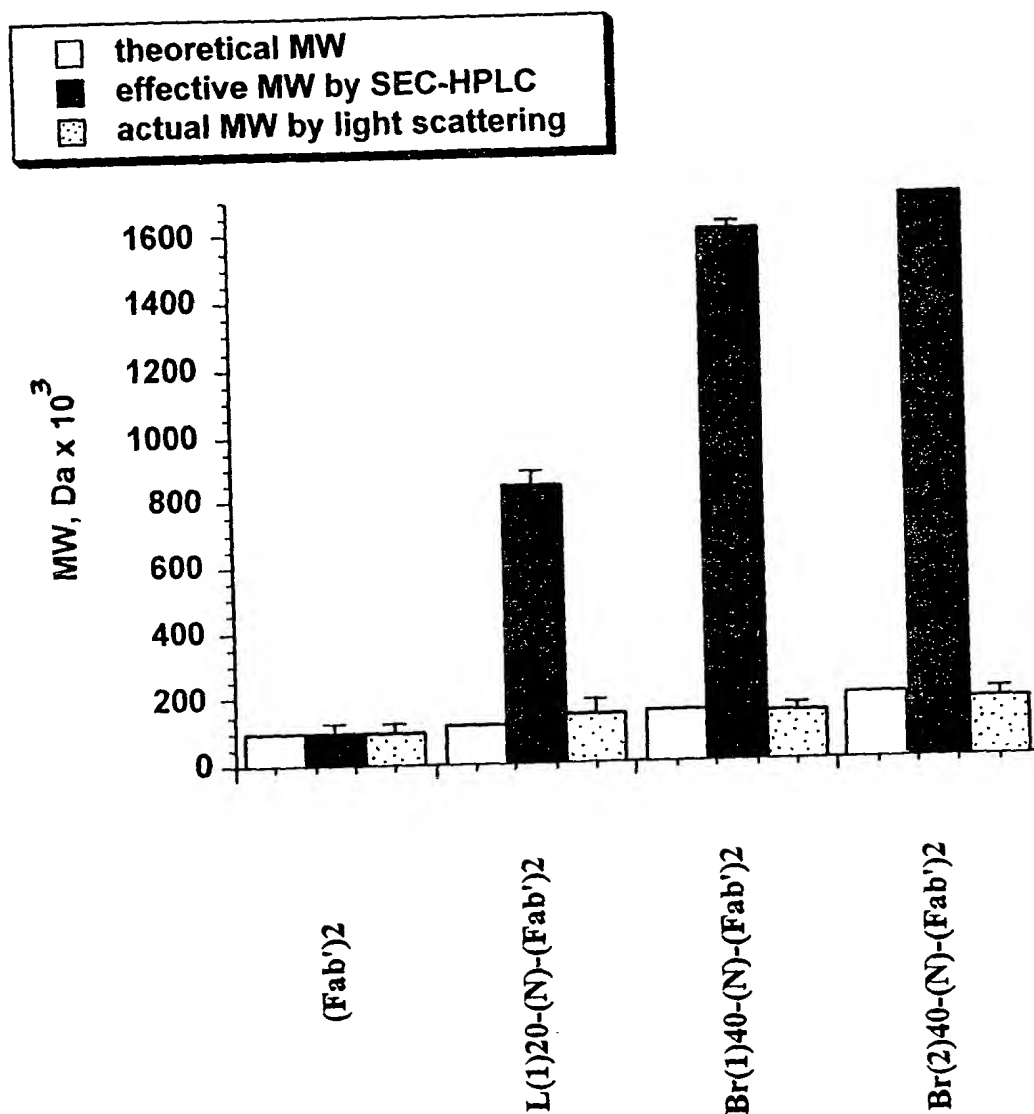


FIG. 63



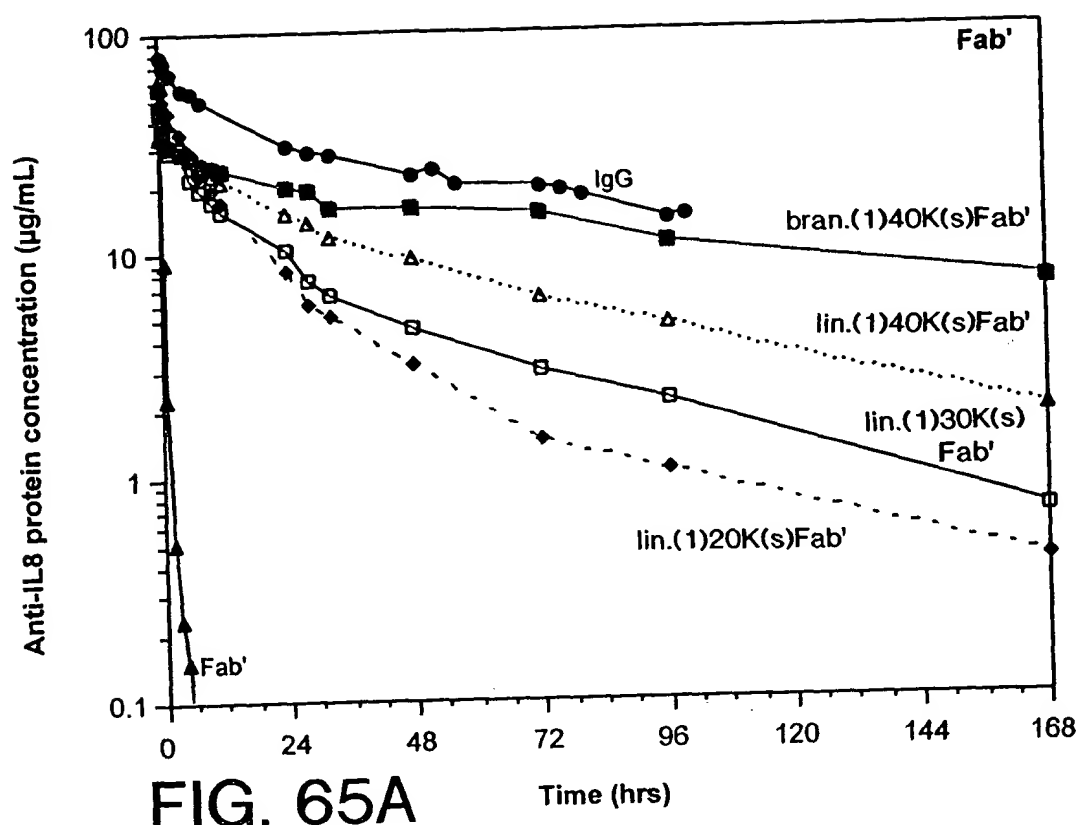


FIG. 65A

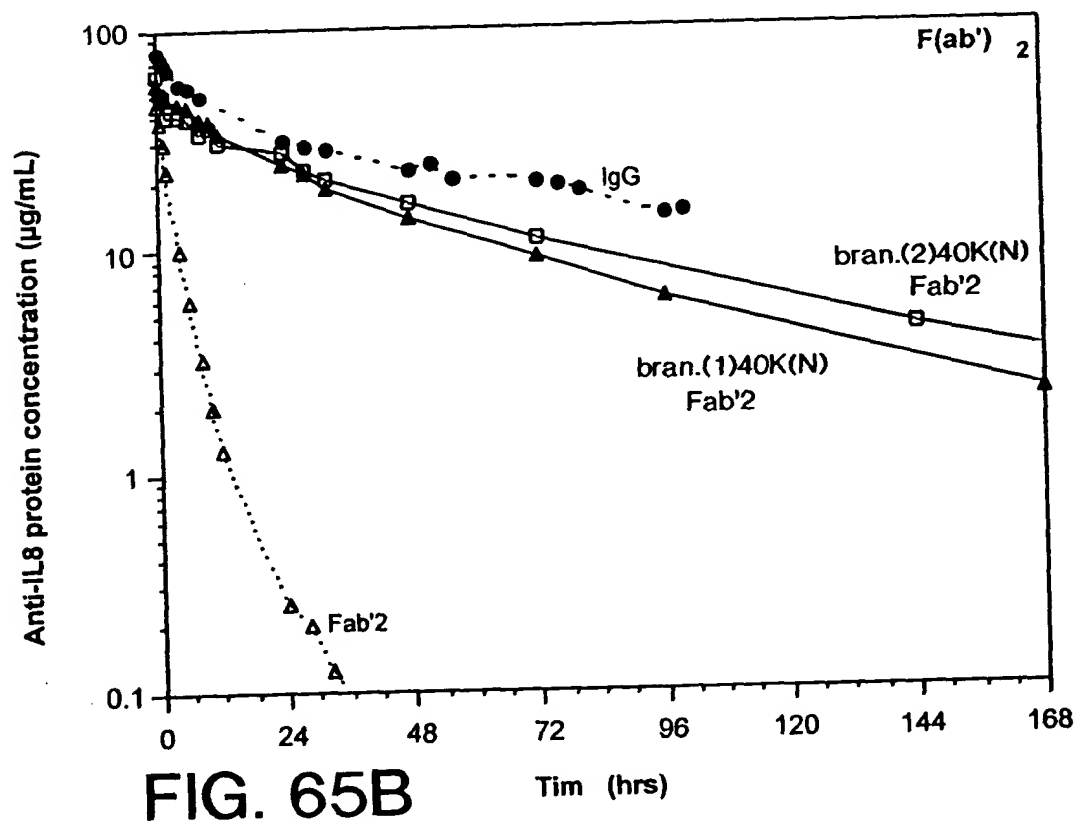


FIG. 65B

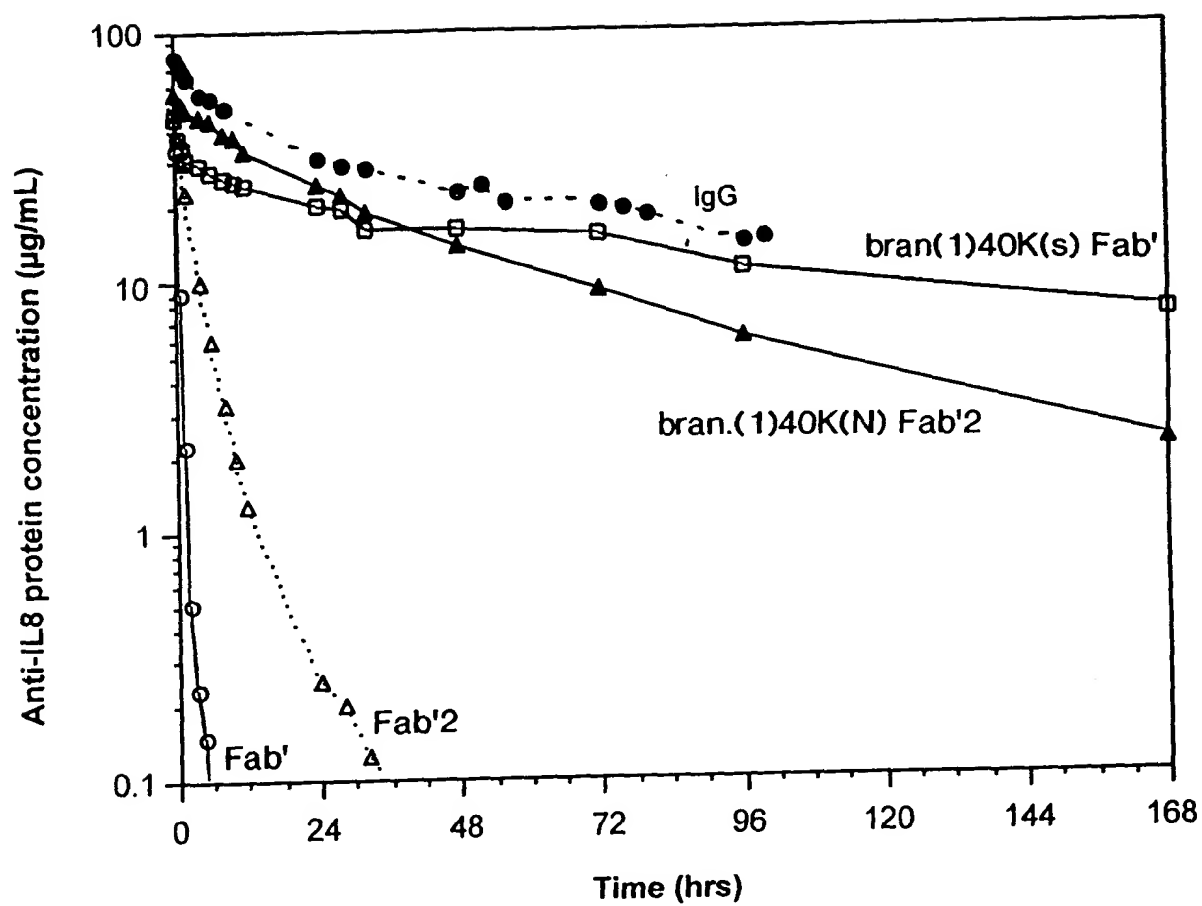


FIG. 66

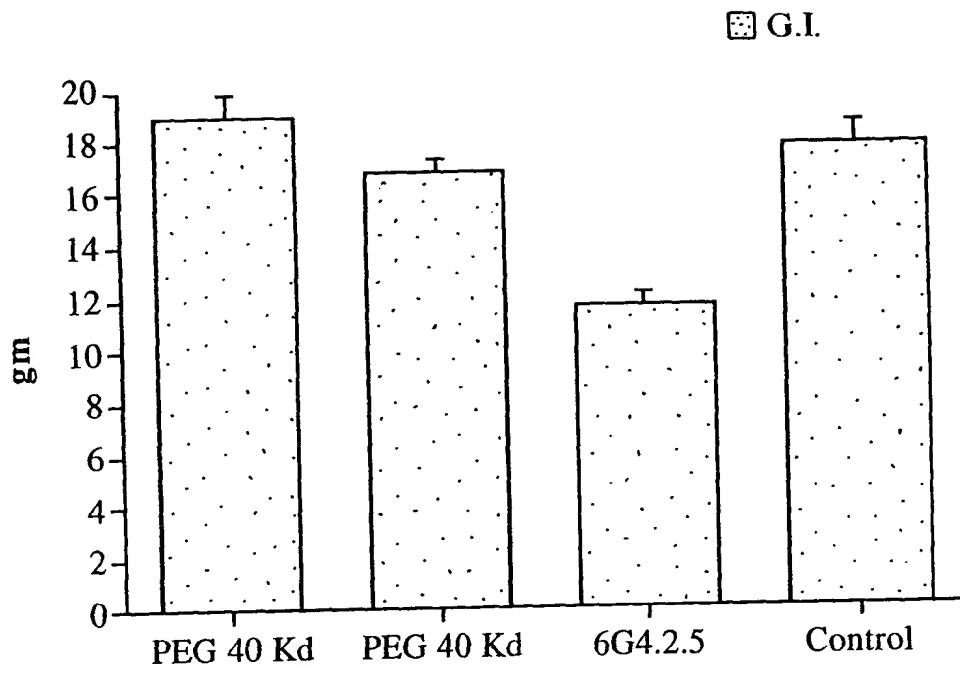


FIG. 67

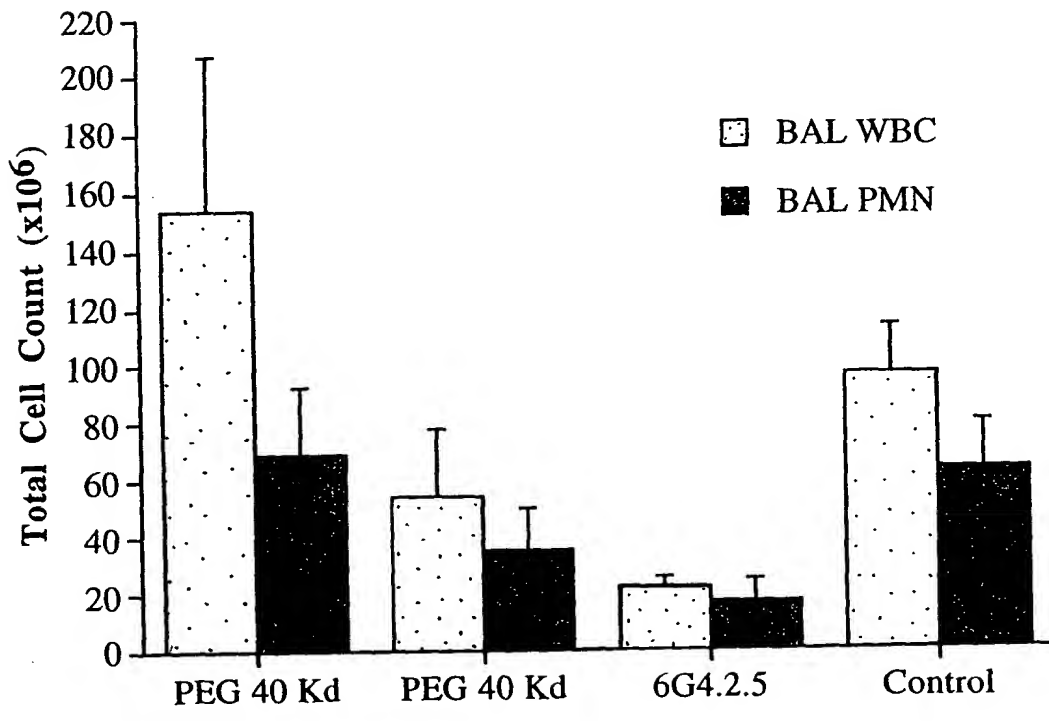


FIG. 68

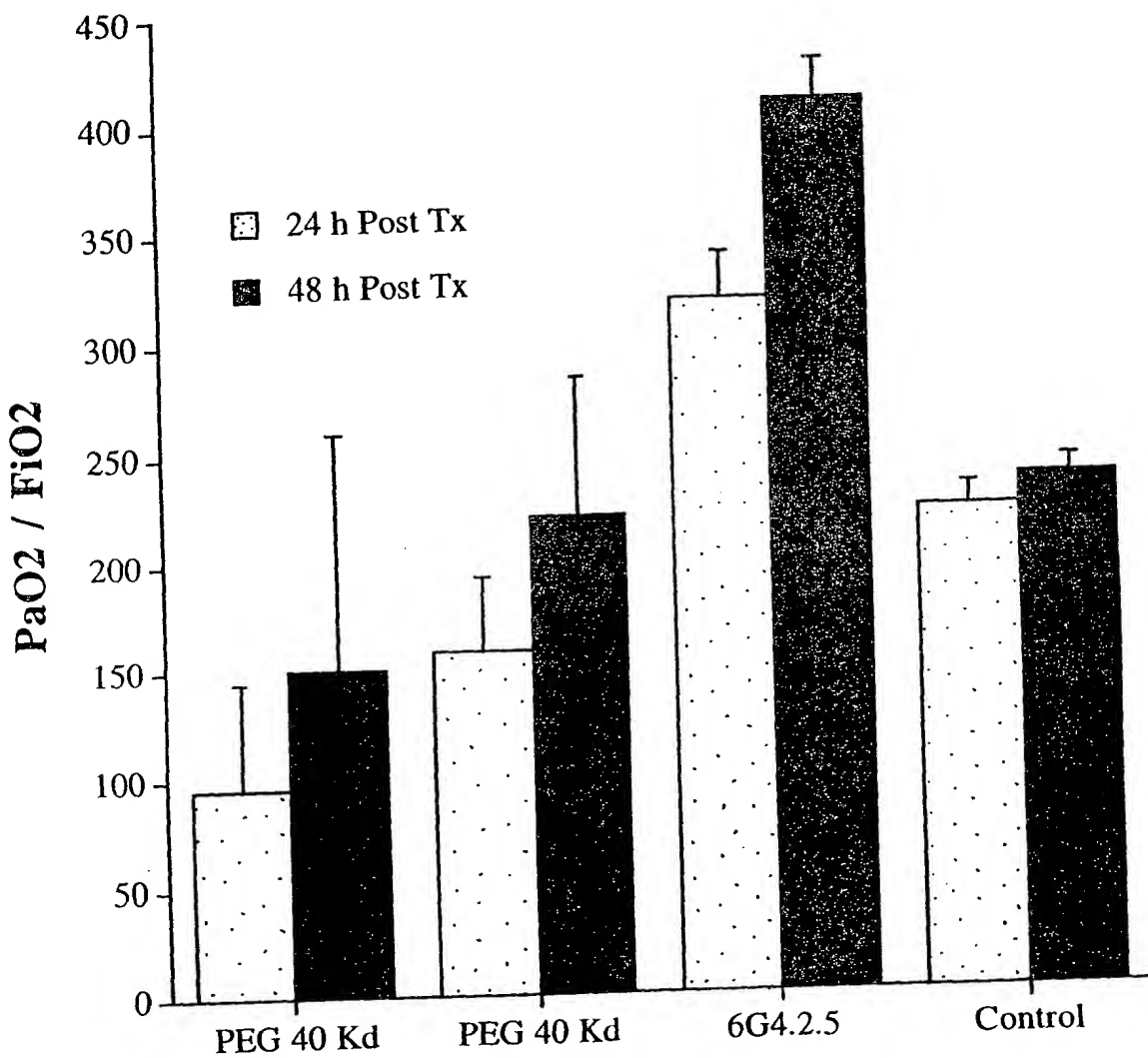


FIG. 69

FIG. 70A

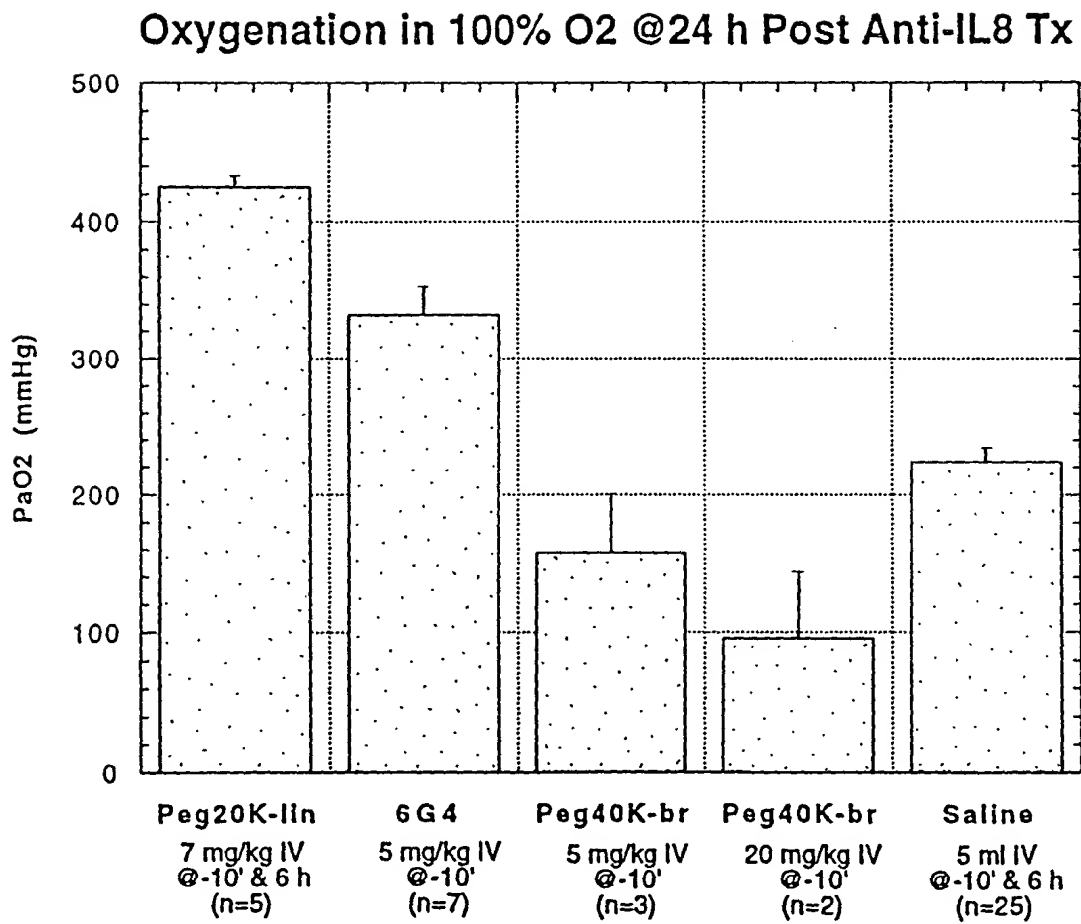


FIG. 70A

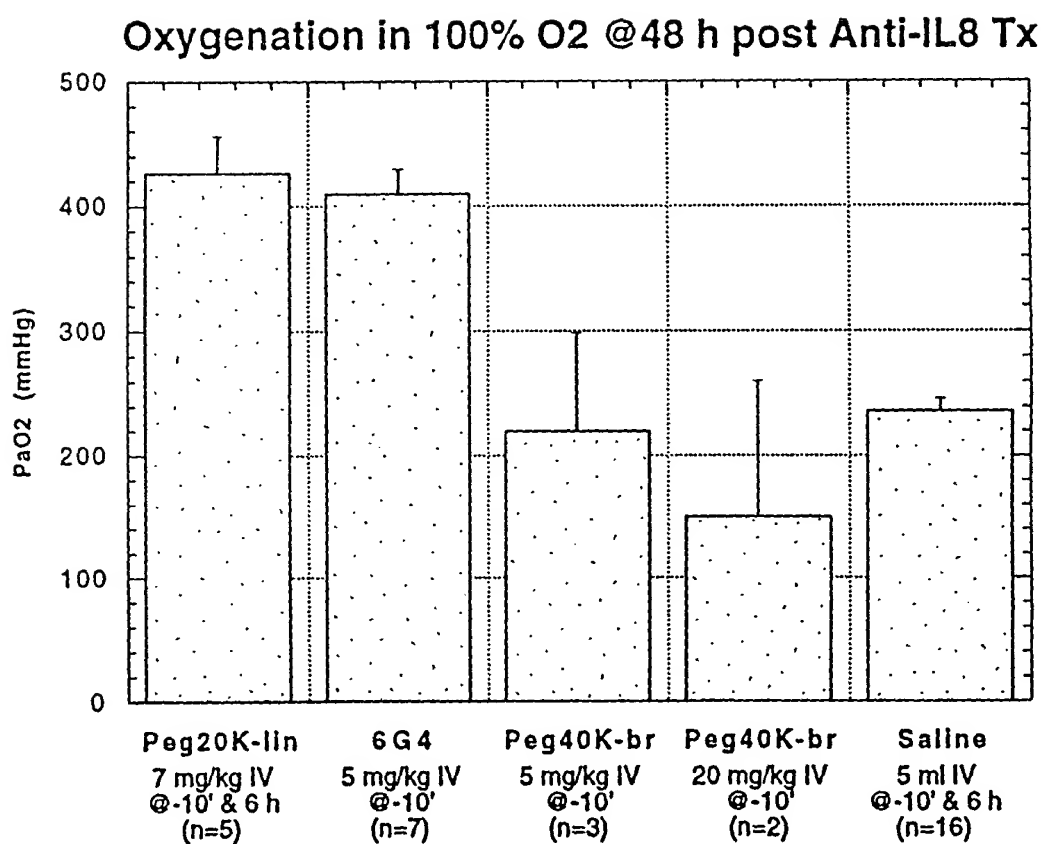


FIG. 70B

FIG. 70C

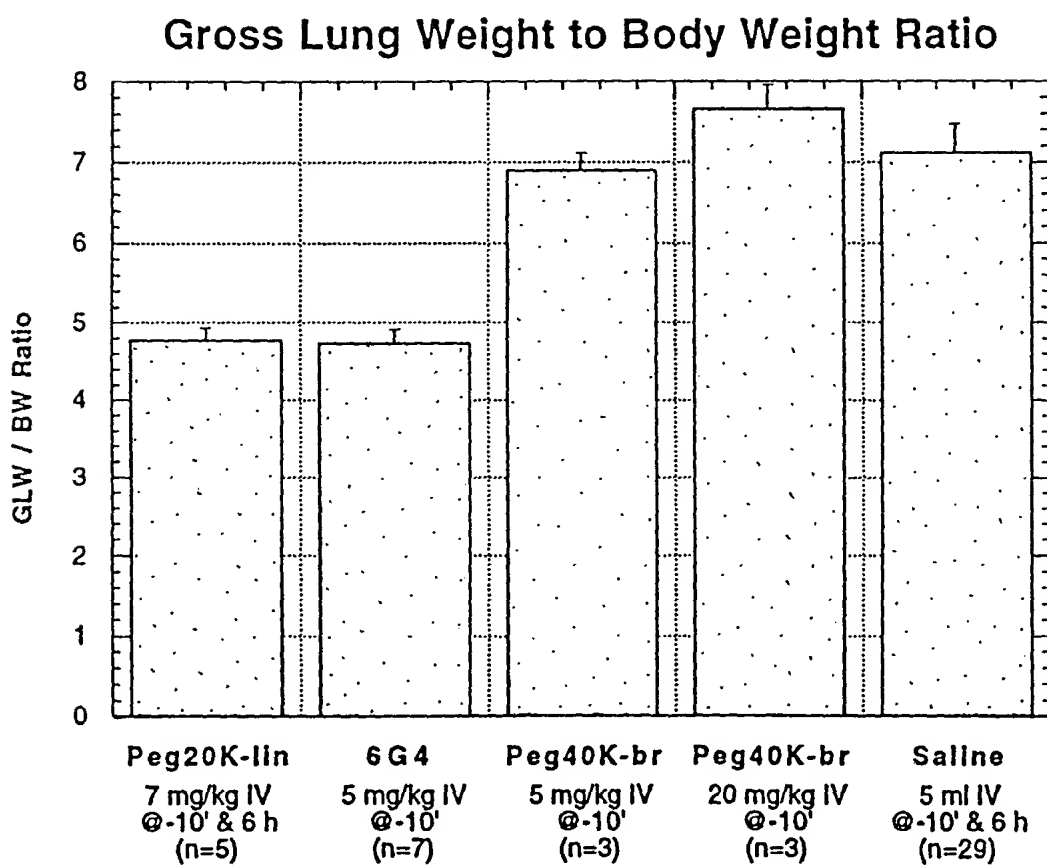


FIG. 70C



FIG. 70D

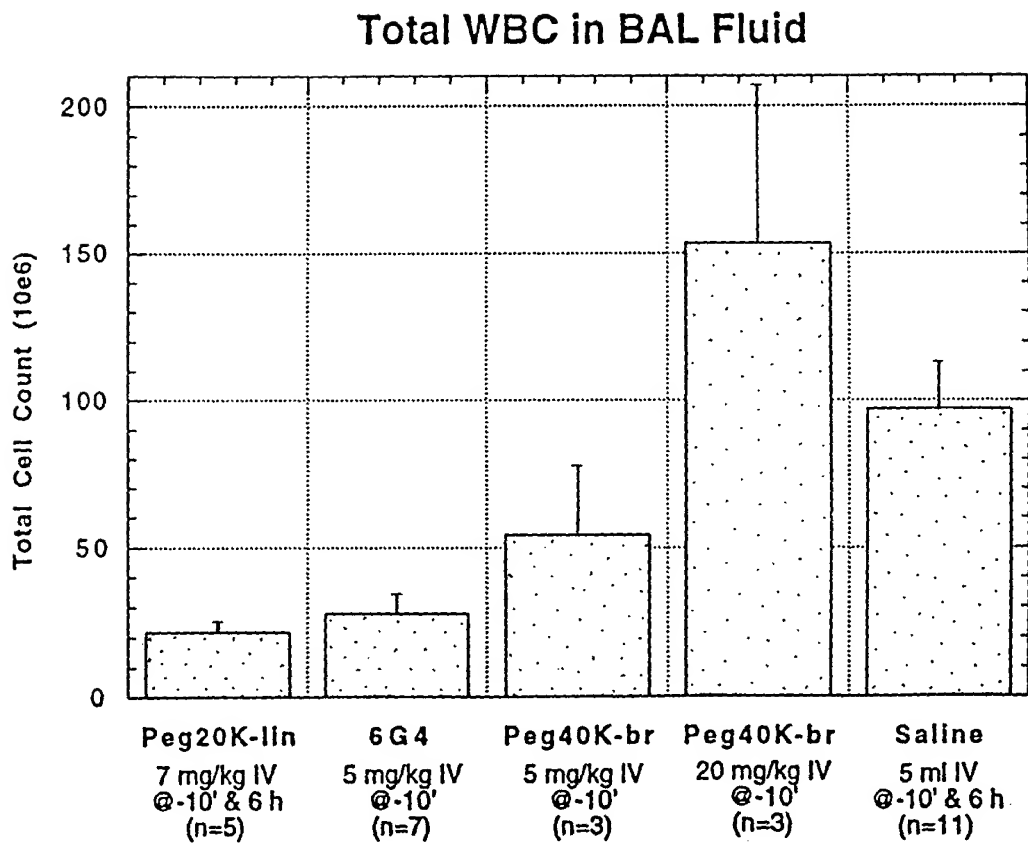


FIG. 70D

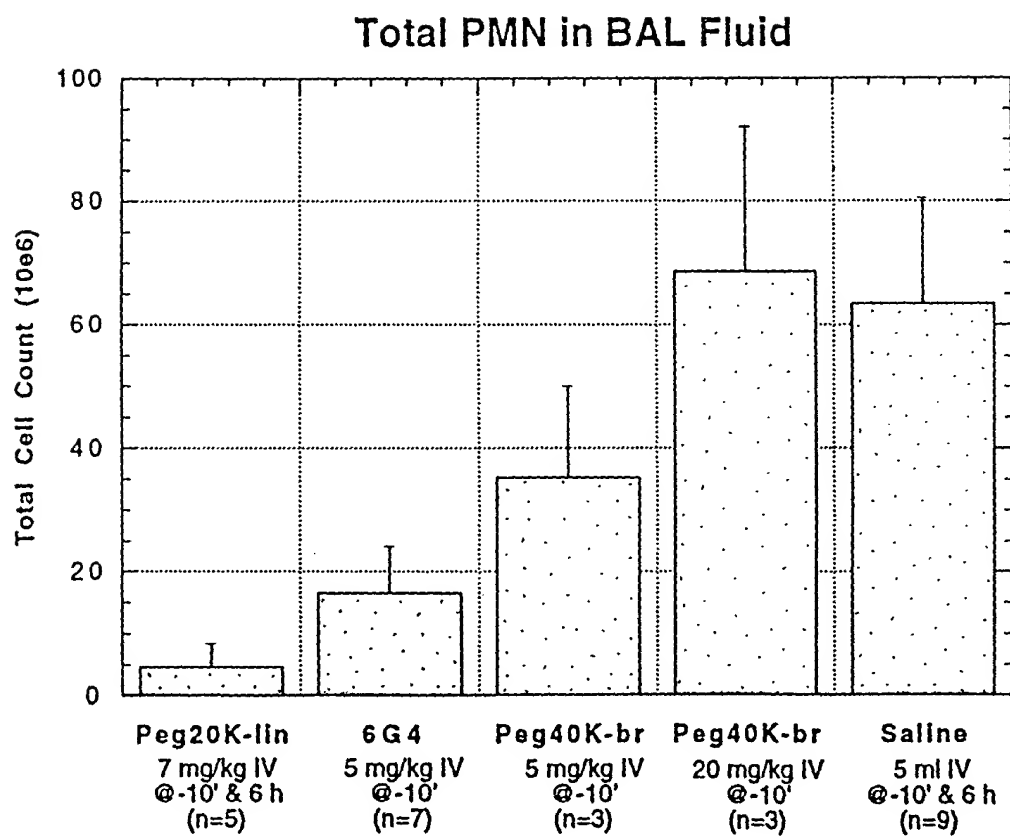
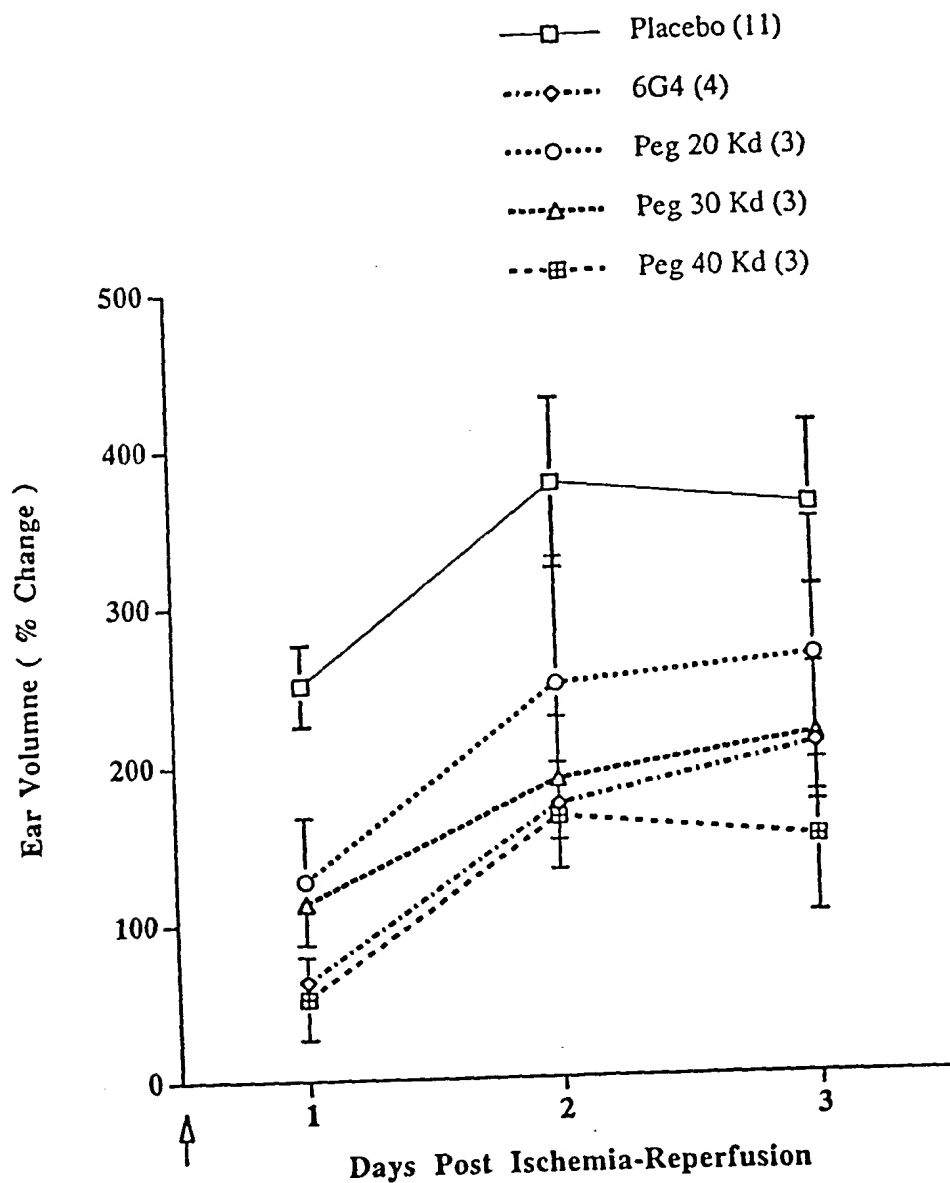


FIG. 70E

The Effect of Pegylated Anti-IL-8 in the Rabbit Ear model of Ischemia-Reperfusion Injury



Anti-IL-8 formulations :
 Single Dose (5 mg/kg)
 administered IV at time
 of reperfusion

FIG. 71